NICE National Institute for Health and Care Excellence

NICE guidance

Avacopan for treating severe active granulomatosis with polyangiitis or microscopic polyangiitis

Technology appraisal guidance
Published: 21 September 2022

www.nice.org.uk/guidance/ta825

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Avacopan with a cyclophosphamide or rituximab regimen is recommended, within its marketing authorisation, as an option for treating severe active granulomatosis with polyangiitis or microscopic polyangiitis in adults. It is recommended only if the company provides it according to the commercial arrangement.

Why the committee made these recommendations

Standard care for granulomatosis with polyangiitis or microscopic polyangiitis usually starts with cyclophosphamide or rituximab, followed by maintenance treatment, usually with azathioprine or rituximab. Corticosteroids are also used throughout treatment. Avacopan is an option to be used alongside this standard care.

Evidence from a clinical trial shows that, after a year, avacopan with standard care is more effective at stopping the conditions getting worse than standard care alone. It also suggests that using avacopan with standard care results in less toxicity from corticosteroids, possibly because of less use overall.

The cost-effectiveness estimates for avacopan with standard care compared with standard care alone are within the range that NICE considers a cost-effective use of NHS resources. So, avacopan with a cyclophosphamide or rituximab regimen is recommended.

2 Information about avacopan

Marketing authorisation indication

2.1 Avacopan (Tavneos, CSL Vifor), 'in combination with a rituximab or cyclophosphamide regimen, is indicated for the treatment of adult patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for avacopan.

Price

2.3 Avacopan costs £5,547.95 per pack of 180x10 mg capsules (company submission). The company has a commercial arrangement. This makes avacopan available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by CSL Vifor, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

Population, treatment pathway and positioning

People with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) can have severe symptoms

3.1 Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is a group of rare autoimmune conditions characterised by blood vessel inflammation. The 2 most common types are GPA and MPA. Eosinophilic GPA is the rarest type of ANCA-associated vasculitis and was not a proposed indication for this appraisal. The patient experts explained that people with GPA or MPA can have severe symptoms and the conditions can be life threatening. They explained that symptoms can include extreme pain, fatigue, night sweats and rashes. They added that ANCA-associated vasculitis can affect the sinuses, kidneys, lungs, abdomen, skin and joints. They also explained that the condition can have a detrimental effect on everyday life, including people's ability to work and participate in family life. The clinical experts commented that, when the kidneys are involved, people can develop end-stage renal disease (ESRD), which can be life threatening. The committee recognised that people with severe active GPA or MPA can have severe symptoms.

People with GPA or MPA, and clinicians, would welcome a new treatment option

3.2 The clinical experts explained that GPA and MPA are usually treated in 2 phases. The first phase aims to control inflammation and reduce damage associated with the conditions by inducing disease remission (see section 3.4). The second phase of treatment (maintenance treatment) aims to prevent the conditions from relapsing and causing

further damage (see section 3.5). Patient and professional organisations commented that quickly inducing and sustaining disease remission are important to reduce the risk of organ damage. The clinical experts agreed that the treatment pathway for people with severe active GPA or MPA is generally well defined. They explained that induction treatment usually includes cyclophosphamide or rituximab with high-dose corticosteroids (usually prednisolone, which is an active metabolite of prednisone). They added that maintenance treatment is usually azathioprine with a tapered dose of corticosteroids. The clinical experts also explained that disease relapses are treated by re-inducing remission in a similar way to initial inductions. Both patient and clinical experts commented on the side effects and toxicity of corticosteroids. The company also noted that relapses are associated with an increased risk of corticosteroid-mediated morbidity. The patient experts commented that mood swings, weight gain, diabetes, osteoporosis and cataracts are all potential side effects of corticosteroid treatment. They explained that weight gain can affect self-confidence and means that some people feel like they no longer recognise themselves. One patient organisation commented that regular monitoring for the side effects by several types of clinicians can be needed. For example, people having corticosteroids for a prolonged time may regularly visit a pain clinic, an ophthalmologist and a rheumatology and orthopaedic combined clinic to manage corticosteroid side effects. One clinical expert commented that infection and cardiovascular disease, which are the most common causes of death in this population, are both associated with corticosteroid use. The clinical experts also commented that the side effects of corticosteroids are generally dose related. So, they explained that a treatment which could sustain disease remission and reduce corticosteroid use would be beneficial. The committee concluded that people with GPA or MPA, and clinicians, would welcome such a new treatment option.

The company's positioning of avacopan is appropriate

3.3 The NICE scope did not specify which types of ANCA-associated vasculitis would be considered in the appraisal. The company explained that only people with GPA or MPA were included in the clinical trial (see section 3.6). It also noted that the marketing authorisation only covered people with severe active GPA or MPA, and specified that avacopan

would be used with a cyclophosphamide or rituximab regimen. The committee recognised that NICE's remit is to appraise a technology within its marketing authorisation, so agreed that the company's positioning was appropriate.

The relevant induction treatment comparators are cyclophosphamide or rituximab with high-dose corticosteroids

3.4 The clinical experts explained that people with severe disease are usually offered cyclophosphamide or rituximab with high-dose corticosteroids for induction treatment. They added that the decision to use rituximab instead of cyclophosphamide depends on many factors. They commented that people with more severe GPA or MPA may be offered cyclophosphamide because there is less evidence for rituximab for severe disease. The clinical experts also commented that anti-CD20 antibody treatments (such as rituximab) can reduce response to vaccinations by depleting B-cells. So, there is a general desire to avoid using these treatments in the context of the COVID-19 pandemic. The committee concluded that the relevant induction treatment comparators were cyclophosphamide or rituximab with high-dose corticosteroids.

The relevant maintenance treatment comparators are azathioprine or rituximab (for people who are eligible) with corticosteroids

3.5 The committee recalled that, after the initial induction treatment, people will usually have maintenance treatment. The clinical experts explained that, after induction of remission with cyclophosphamide, most people would switch to azathioprine. The clinical experts also noted that, during the maintenance phase of treatment, corticosteroid dose is usually tapered. They explained that people who initially have rituximab induction would only have rituximab maintenance in specific circumstances, in accordance with the NHS Clinical Commissioning Policy on rituximab for treating ANCA-associated vasculitis in adults. This states that rituximab maintenance is only commissioned if the disease has relapsed and re-induction treatment is needed after rituximab-induced remission or if rituximab is needed to induce remission for

cyclophosphamide-refractory disease. The clinical experts commented that, in clinical practice, around 30% to 40% of people who have had rituximab as induction treatment have rituximab maintenance treatment. People who are not eligible for rituximab maintenance treatment would have azathioprine instead. The committee concluded that the relevant maintenance comparators were azathioprine with tapered corticosteroids and rituximab with tapered corticosteroids.

Clinical effectiveness

Avacopan with a cyclophosphamide or rituximab regimen is effective in sustaining disease remission and reducing corticosteroid toxicity

3.6 The company provided clinical evidence for avacopan from several clinical trials including ADVOCATE, a phase 3 trial. ADVOCATE was a randomised, active-controlled trial comparing oral avacopan 30 mg twice daily with oral prednisone on a tapering schedule. Everyone also had either cyclophosphamide followed by azathioprine, or rituximab followed by nothing. The trial included people with a clinical diagnosis of GPA or MPA who had at least 1 major item, 3 minor items or 2 renal items of proteinuria and haematuria on the Birmingham Vasculitis Activity Score (BVAS). The primary endpoint was the proportion of people with disease remission at weeks 26 and 52. At week 26, disease remission was defined as a BVAS of 0, and no corticosteroids in the previous 4 weeks. Sustained remission was defined as disease remission at week 26, and a BVAS of 0 at week 52, no corticosteroids in the 4 weeks before week 52 and no disease relapse between weeks 26 and 52. In the intention-to-treat population, at week 26, 72% of people in the avacopan group compared with 70% in the prednisone group had disease remission (estimated common difference 3.4%, 95% confidence interval [CI] -6.0 to 12.8; $p<0.001$ for non-inferiority and $p=0.240$ for superiority). At week 52, 66% of people in the avacopan group compared with 55% in the prednisone group had sustained disease remission (estimated common difference 12.5%, 95% CI 2.6 to 22.3; $p<0.001$ for inferiority and $p=0.007$ for superiority). The trial also evaluated corticosteroid toxicity. At week 26, the mean Corticosteroid Toxicity Index Cumulative Worsening

Score was 39.7 in the avacopan group compared with 56.6 in the prednisone group (a larger score represents worsening toxicity; p=0.0002). The committee concluded that avacopan with a cyclophosphamide or rituximab regimen was effective at sustaining disease remission and reducing corticosteroid-induced toxicity compared with a prednisone-based regimen in the intention-to-treat population of ADVOCATE.

In ADVOCATE, non-study supplied corticosteroids in the intervention group reflect expected use in clinical practice

3.7 In ADVOCATE, people in both the avacopan and prednisone groups could have non-study supplied corticosteroids as needed. This was, for example, to treat disease relapse or hypoadrenalism from previous use of high-dose corticosteroids. The company explained that this as-needed use of corticosteroids was in line with how they would be used in clinical practice if avacopan was available. The clinical experts agreed. The mean cumulative corticosteroid dose during the treatment period was 1,349 mg in the avacopan group compared with 3,655 mg in the prednisone group. The ERG noted that although total corticosteroid use was lower in the avacopan group, non-study supplied corticosteroid use was higher in the avacopan group. The mean non-study supplied corticosteroid use during the treatment period was 1,349 mg in the avacopan group compared with 1,265 mg in the prednisone group. The ERG also noted that a large proportion of people (87.3%) in the avacopan group had non-study supplied corticosteroids during the treatment period. It was concerned that the use of non-study supplied corticosteroids in the avacopan group could have biased the effect estimates from the trial. It was also concerned about the meaningfulness of the apparent comparison of avacopan with lower-dose corticosteroids compared with higher-dose corticosteroids. The company explained that non-study supplied corticosteroid use was reasonably well balanced between the avacopan and prednisone groups, so the benefits seen in ADVOCATE could be attributed to avacopan. The committee understood the ERG's concerns, and queried whether there were differences in the proportions of people who had pulsed high-dose corticosteroids. One clinical expert explained that most non-study supplied intravenous corticosteroids at 4 weeks were for prophylaxis for rituximab treatment

rather than for treating relapse. The committee commented that, overall, people in the avacopan group had about one-third less corticosteroids than those in the prednisone group. The committee recalled that a reduction in corticosteroid use would be beneficial for people with GPA or MPA (see section 3.2). It concluded that the non-study supplied corticosteroids in the intervention group reflected expected use in clinical practice.

Cost effectiveness

The company's economic model is appropriate for decision making

3.8 The company provided a Markov model that was similar to the one used in NICE's technology appraisal guidance on rituximab in combination with glucocorticoids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis. The model included 9 health states: active disease, 3 disease-remission states, 3 disease-relapse states, ESRD and death. The cohort's mean starting age (60 years), proportion of people having rituximab induction treatment (65%) and adherence to avacopan (86%) were from ADVOCATE. The clinical efficacy for avacopan was based on the results of ADVOCATE, and included disease remission at 26, 52 and 60 weeks, change in estimated glomerular filtration rate (eGFR) and health-related quality of life. In the company's base case, people were modelled to have standard care or standard care with avacopan. Standard care was defined as high-dose corticosteroids and either cyclophosphamide or rituximab followed by lower-dose corticosteroids with azathioprine. The company explained that modelling azathioprine maintenance treatment after rituximab induction was a deviation from ADVOCATE, but was based on an assumption explored in NICE's technology appraisal guidance on rituximab. At the first meeting, the committee was concerned about how maintenance treatment was modelled (see section 3.9). But it concluded that the company's overall model structure was appropriate for decision making.

The cost-effectiveness analysis should include rituximab

maintenance treatment for people who are eligible for it

3.9 The committee recalled that some people are eligible to have rituximab in the maintenance phase if it was used in the induction phase and other criteria are met (see section 3.5). The company noted that there were no randomised controlled trials assessing maintenance treatment with avacopan plus rituximab. At clarification, the company provided a rituximab maintenance treatment option in the model. It explained that it had adjusted the baseline hazard ratio for relapse to reflect treatment with rituximab instead of azathioprine. It cautioned that the non-adjusted naive comparison should be treated as exploratory. The ERG commented that the rituximab maintenance scenario was uncertain. At the first meeting, the committee agreed that it would have preferred analyses in which 30% to 40% of people who had rituximab as induction treatment continued rituximab as maintenance treatment, with the remaining proportion having azathioprine. This was based on the clinical experts' comments (see section 3.5). In response to consultation, the company updated its base case to include rituximab maintenance treatment for 35% of people who had it as induction treatment. It also provided scenarios that assumed 30% and 40% of this population would continue to have rituximab. The company noted that there was no additional real-world evidence to inform the modelling. The ERG commented that, in the absence of real-world observational data, the company's naive approach was pragmatic. The committee concluded that the company's modelling of rituximab maintenance treatment was appropriate and considered all scenarios during decision making.

Hazard ratios for ESRD from Gercik et al. and Brix et al. are relevant both individually and pooled

3.10 In the company's model, people could transition to an ESRD state. The company considered it relevant to include a separate health state because ESRD is a significant complication of ANCA-associated vasculitis. Disease progression to ESRD was modelled by a change in eGFR. The probability of ESRD in the active and remission health states was adjusted based on the improvement in eGFR in ADVOCATE. In the company's base case, the hazard rate, and probability of ESRD was adjusted based on the hazard ratio for ESRD per ml/min change in eGFR

from Gercik et al. (2020; hazard ratio [HR] 0.90, 95% CI 0.86 to 0.95). However, the ERG noted that the company had provided several other options for the hazard ratio in the model. The ERG originally explored a pooled hazard ratio by combining estimates from Gercik et al., Ford et al. (2014) and Brix et al. (2018). The company disagreed with the ERG's pooled approach, explaining that estimates from Cox proportional hazards models were dependent on other covariates in the model. It explained that it would be inconsistent to pool coefficients from models that adjust for different covariates. During technical engagement, the ERG noted the company's concerns about pooling estimates. It re-evaluated the pooled studies and noted that the estimate from Ford et al. was for ESRD or death. The ERG did not consider it appropriate to include the Ford et al. hazard ratio in the pooled estimate. But the ERG reiterated that both the Gercik et al. and Brix et al. studies were relevant and preferred to pool them using an inverse variance approach (pooled HR 0.95, 95% CI 0.90 to 1.00). The committee understood the company's statistical concerns about pooling estimates. However, it agreed with the ERG that both the Gercik et al. and Brix et al. studies were relevant for consideration. The committee noted that the Gercik et al. study did not provide much detail and was published as a letter. It further noted comments from a clinical expert that the risk of ESRD is dependent on the population being studied. This meant that it may have been appropriate to pool estimates from studies that limited the inclusion criteria. The committee was concerned that the company's approach might have applied a hazard ratio from a single study with a narrower population to the broader, modelled population. The committee would have liked to see additional information from the company about why Brix et al. was not relevant. At the first meeting, the committee concluded that it was relevant to consider scenarios using the Gercik et al. and Brix et al. hazard ratios, both individually and pooled. In response to consultation, the company updated its base case to use the pooled hazard ratio estimated by the ERG (HR 0.95). The company commented that the pooled approach was conservative because evidence from the Gopaluni et al. (2019) paper suggested that the true hazard ratio could be less than 0.95 but was likely greater than 0.90. Consistent with the committee's preference from the first meeting, the company also provided results using the Gercik et al. and Brix et al. estimates individually. The committee noted that the incremental cost-

effectiveness ratio (ICER) was sensitive to the individual and pooled hazard ratios. No evidence had been presented to suggest either Gercik et al. or Brix et al. estimates were not relevant. So, the committee concluded that the company's analyses using the individual and pooled estimates were relevant for decision making.

The 2019/20 NHS reference costs are most appropriate to inform hospitalisation costs

3.11 The company noted that the average length of hospital stay in ADVOCATE (13.8 days in the avacopan group and 19.6 days in the prednisone group) was longer than the mean length of stay reported in the 2019/20 NHS reference costs. The company explained that it adjusted hospital costs to account for the longer stays in ADVOCATE using excess bed day costs from 2017/18. It did this because the 2019/20 NHS reference costs no longer separately report excess bed day costs (as previous versions did). At technical engagement, the company updated its base case to use unit and excess bed day costs from 2017/18 inflated to 2020 prices. The ERG explained that it was uncertain whether the difference between mean length of stay in ADVOCATE compared with NHS reference costs implied excess bed days. Additionally, the ERG noted that NHS reference costs appeared to be calculated differently between 2017/18 and 2019/20 because the more recent version does not separately report excess bed day costs. NHS England confirmed that the 2019/20 reference costs included all hospitalisation costs, but no longer disaggregated costs into unit and excess bed days. At the first meeting, the committee noted a preference for hospitalisation costs using 2019/20 unit costs with no adjustment for excess bed days. This was because it was more reflective of costs in the NHS in England. In response to consultation, the company updated its base case to use 2019/20 unit costs with no adjustment for excess bed days. The company noted this approach was conservative because:

- the unit cost represents the average length of stay and does not reflect the long hospital stays seen in ADVOCATE

- the average length of stay from the NHS reference costs includes overall ANCA-associated vasculitis, rather than the narrower population with severe active GPA or MPA for which avacopan is indicated.

  The committee concluded that the company's revised approach to hospitalisation costs using 2019/20 unit costs with no adjustment for excess bed days was appropriate for decision making.

The modelled healthcare costs may not fully represent costs in the NHS, but may be conservative

3.12 The ERG noted the crude modelled annual healthcare costs for the standard care group were substantially lower than the costs in the Clinical Practice Research Datalink (CPRD) study. The CPRD study was a retrospective observational study using real-world evidence to evaluate resource use and adverse event rates for people with GPA or MPA in England. The company explained that the CPRD study costs were not appropriate for modelling because there is no information about change in resource use with avacopan. The company also noted that the CPRD included aggregate costs of all hospital episodes, including treatment of unrelated comorbidities, and the model did not account for these costs. The company added that costs for specific episodes were similar between the model and CPRD. It also explained that larger costs from worsening ANCA-associated vasculitis would favour avacopan so the model was likely conservative. The ERG noted it was uncertain why the ICER increased when adverse event costs from CPRD were used. It explained that it was not possible to explore the CPRD data further because the database included limited detail on exact resource use and did not include people who had avacopan treatment. At the second committee meeting, the committee noted that the CPRD study may have underrepresented people with MPA. People with MPA are more likely to have renal involvement so there may be higher costs associated with their care because they have high-cost treatments such as dialysis. The committee recalled that higher costs for the standard care group would favour avacopan because it is effective at sustaining disease remission, reducing ESRD and reducing corticosteroid use and so toxicity. The committee concluded that although there was some uncertainty in the modelled healthcare costs, the company's base case was appropriate

and likely conservative.

Cost-effectiveness estimate

Avacopan with a cyclophosphamide or rituximab regimen compared with standard care is cost effective

3.13 The committee recalled that its preferred assumptions were:

- that 30% to 40% of people who have rituximab induction treatment would have it as maintenance treatment (see section 3.9)
- that the Gercik et al. (2020) and Brix et al. (2018) estimates for the ESRD hazard ratio were relevant individually and pooled (see section 3.10)
- 2019/20 NHS reference costs for hospitalisation costs with no adjustment for excess bed days (see section 3.11).

The committee recognised that the company and ERG had the same base case. This included an assumption that 35% of people who had rituximab induction treatment continued it as maintenance treatment, and a pooled hazard ratio for ESRD that reflected its preferred assumptions. The committee also considered scenarios in which 30% and 40% of people had rituximab maintenance, and in which the individual hazard ratio estimates for ESRD were used. The committee recognised that, although there was inherent uncertainty associated with some assumptions, most were conservative. So, it thought that it was reasonable to assume that the ICER would decrease if it were possible to resolve these issues. The committee also recognised that the quality-adjusted life year (QALY) gains were relatively stable, and that GPA and MPA are rare, so considered the consequences of decision error to be relatively low. It concluded that the most plausible ICER was within the range NICE normally considers an acceptable use of NHS resources (that is, £20,000 to £30,000 per QALY gained). The exact ICER cannot be reported here because it includes confidential discounts for some of the comparator treatments. The committee concluded that avacopan with a cyclophosphamide or rituximab regimen is a cost-effective use of NHS resources compared with standard care alone.

Other factors

There are no equality issues to address in this technology appraisal

3.14 The committee understood a potential equality issue about the use of cyclophosphamide had been raised in NICE's related technology appraisal guidance on rituximab. In that appraisal, the committee considered that cyclophosphamide reduces fertility in everyone. But it was aware that the peak age of onset for ANCA-associated vasculitis in England is between 60 and 70 years. The committee agreed that the number of people with ANCA-associated vasculitis who have not completed their family is likely to be very small. The committee recalled that avacopan is proposed as an add-on to standard care. It considered that its recommendation for avacopan would not affect prescription rates for cyclophosphamide. So, it concluded that its recommendation for avacopan would not have a different effect on people protected by the equality legislation than on the wider population.

There may be additional benefits of avacopan not captured in the cost-effectiveness analysis

3.15 The committee recalled that, during the COVID-19 pandemic, clinicians are being careful about using anti-CD20 antibody treatments (like rituximab, see section 3.4). It also recalled that avacopan was proposed as an add-on to standard care so would not directly replace rituximab. But it also considered that a larger proportion in the avacopan group had sustained remission at week 52 than in the prednisone group. The clinical experts explained that a drug that could maintain disease remission may reduce future need for re-induction treatment with rituximab. The committee also recognised that the model mainly captured benefits of disease remission rather than the potential health benefits from a long-term reduction in corticosteroids. The committee concluded that there may be some benefits of avacopan not captured in the cost-effectiveness analysis. These included reducing the future need for rituximab and a long-term reduction in corticosteroid use. It took these factors into consideration when making its recommendation.

Conclusion

Avacopan with a cyclophosphamide or rituximab regimen is recommended for treating severe active GPA or MPA in adults

3.16 The committee recalled that GPA and MPA are rare, severe and potentially life-limiting conditions. It recognised that current treatment usually includes corticosteroids, which are associated with significant side effects. The committee understood that people with severe active GPA or MPA would welcome a treatment option that could reduce corticosteroid use and its associated toxicity. It recognised that avacopan with a cyclophosphamide or rituximab regimen compared with standard care sustained disease remission for a larger proportion of people, and reduced corticosteroid-induced toxicity. The committee noted that, after consultation, the company and ERG agreed on all assumptions. It also noted that these assumptions were consistent with the committee's preferences. These included:

- that 35% of people who had induction treatment with rituximab had it as maintenance treatment
- a pooled hazard ratio for ESRD
- hospitalisation costs based on 2019/20 NHS reference costs with no adjustment for excess bed days.

It also acknowledged there may be additional benefits for avacopan that had not been captured in the cost-effectiveness analysis (see section 3.15). The committee considered the most plausible ICER was within the range that NICE normally considers a cost-effective use of NHS resources. So, avacopan is recommended for treating severe active GPA or MPA.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has severe active granulomatosis with polyangiitis or microscopic polyangiitis and the doctor responsible for their care thinks that avacopan is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

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ISBN: 978-1-4731-4708-9

Accreditation