benralizumab solution for injection in pre-filled pen (Fasenra®)

AstraZeneca UK Limited

05 June 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

benralizumab (Fasenra®) is accepted for use within NHSScotland.

Indication under review: As an add-on treatment for adult patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA).

Evidence from a randomised, double-blind, phase III study demonstrated that add-on treatment with benralizumab was non-inferior to mepolizumab at achieving remission at both week 36 and 48. Indirect treatment comparisons suggested that benralizumab plus standard of care (SoC) is associated with higher remission rates than SoC alone.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Benralizumab is a humanised monoclonal antibody which binds specifically to the alpha subunit of the human interleukin-5 receptor (IL-5Rα) expressed on the surface of eosinophils. Benralizumab signals through immune effectors cells which leads to apoptosis of eosinophils through enhanced antibody-dependent cell-mediated cytotoxicity; this reduces the eosinophilic inflammation that is characteristic of EGPA.[1, 2]

The recommended dose of benralizumab for this indication is 30 mg by subcutaneous injection every 4 weeks. Benralizumab is intended for long-term treatment. A decision to continue the therapy should be made at least annually based on disease severity, level of disease control and blood eosinophil counts. Patients who develop life-threatening manifestations of EGPA should be evaluated for the need for continued therapy, as benralizumab has not been studied in this population.[1]

1.2. Disease background

Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss syndrome, is a rare, systemic, necrotising vasculitis of small- to medium-sized vessels which ultimately results in damaged organs and tissues; the upper and lower airways are most commonly affected.[2, 3] The majority (74 % to 100 %) of patients with EGPA have asthma at diagnosis, driven by the high levels of eosinophilic inflammation. The asthma is typically severe (in approximately 50 % to 60 % of patients) and corticosteroid dependent.[2, 4-6] Chronic rhinosinusitis (with or without nasal polyposis) is also predominant feature of EGPA. Later symptoms of EGPA include rashes, joint pain and swelling, peripheral neuropathy, abdominal pain, diarrhoea, shortness of breath, arrhythmia, chest pain and heart failure.[3]

In the UK, the estimated prevalence of EGPA is between 23 to 46 cases per 1,000,000 [7]; this means that approximately 200 people in Scotland are affected. The average age at diagnosis is around 50 years[2]; however, diagnosis is difficult and delays of years are common which can result in greater disease severity.[3] Conventional therapy for EGPA allows for high overall survival rates (cumulative survival rates at 10 years from disease onset are above 75 %).[2, 3]

1.3. Treatment pathway and relevant comparators

Current standard of care (SoC) for EGPA is oral corticosteroids, with or without immunosuppressants (such as azathioprine, methotrexate, and mycophenolate mofetil); SoC is the relevant comparator for this submission. If EGPA is severe (organ- or life-threatening), cyclophosphamide and rituximab are also options to induce remission; however, these are not relevant comparators for this submission. The main goal of EGPA treatment is to induce and then maintain remission.[3, 8] Once remission is achieved, corticosteroids should be tapered to the lowest effective dose to reduce the risk or impact of steroid-related side effects.[3, 8] However, relapses are common during tapering and prolong the process.[8]

Mepolizumab is licensed for this indication (add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory EGPA)[9] but it is not recommended for use by SMC due to

non-submission (SMC2490). Clinical experts consulted by SMC advised that mepolizumab is not used in Scottish clinical practice for EGPA.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the use of benralizumab for this indication comes from the MANDARA study. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant study.[2, 10]

Criteria	MANDARA
Study design	International, randomised, double-blind, parallel group, phase III, non-inferiority study.

Eligible patients	• Aged 18 years or older, with a documented EGPA diagnosis of at least 6 months prior to screening, based on the history or the presence of: asthma plus documented blood eosinophilia (eosinophil count of > 1.0 x 10^9/L and/or > 10 % of leukocytes) plus documentation of at least two additional features of EGPA.
	• History of relapsing or refractory EGPA disease:
	  ○ Relapsing disease: at least one confirmed EGPA relapse[a] within the past 2 years, which occurred ≥ 12 weeks prior to screening, whilst receiving an OCS dose of ≥ 7.5 mg per day.
	  ○ Refractory disease: no supportive remission (see below) within the 6 months prior to screening following induction treatment with a standard regimen (for at least 3 months); OR a recurrence of EGPA symptoms within the 6 months prior to screening whilst tapering OCS, occurring at any dose level ≥ 7.5 mg/day OCS.
	• Stable OCS therapy (7.5 mg to 50 mg per day), with or without stable immunosuppressant therapy (excluding cyclophosphamide), for at least 4 weeks prior to baseline.

Treatments and randomisation	Patients were randomised equally to receive benralizumab 30 mg or mepolizumab 300 mg, administered subcutaneously every 4 weeks. The 52-week double-blind period consisted of a 48-week treatment period and a 4-week follow-up period. All patients who completed the 52-week double-blind period were eligible to continue into the OLE, where all patients were treated with open-label benralizumab and were followed up for at least one year. Patients continued on their prior EGPA OCS, and immunosuppressants if applicable during the study; the OCS dose was tapered at the discretion of the investigator throughout the study. Randomisation was stratified according to region (North America, Western Europe, Japan).
Primary outcome	Two definitions of remission were assessed in the study: • **Main remission:** defined as a BVAS = 0 and a reduction in OCS dose to ≤ 4 mg per day). • **Supportive remission:** defined as a BVAS = 0 and a reduction in OCS dose to ≤ 7.5 mg per day). The primary outcome was the proportion of patients who achieved main remission at both weeks 36 and 48. A supportive primary outcome, was the proportion of patients who achieved supportive remission at both weeks 36 and 48. The BVAS is a clinician-completed tool, that is divided into nine organ-based systems, to assess clinically active vasculitis that would likely require treatment, after exclusion of other causes. The BVAS score ranges from 0 to 63, with higher scores reflecting more severe disease. Note that even a score of 1 is indicative of active disease.
Selected Secondary outcomes	• Average daily dose of OCS during week 48 through week 52. • Reduction from baseline in average daily dose of OCS during week 48 through week 52. • Annualised relapse rate. • Change from baseline to week 52 in ACQ-6 (to assess asthma symptom changes).

	• Change from baseline to week 52 in SNOT-22 (to assess sinonasal symptom changes).
Statistical analysis	All efficacy analyses were performed in the full analysis set (FAS); this included all patients who were randomised and received at least one dose of treatment during the double-blind period, irrespective of their protocol adherence and continued participation in the study. At the primary analysis (August 2023 data cut-off): a prespecified non-inferiority margin of–25 % with a one sided 2.5 % significance level was used, in the FAS population. The lower bound of the 95 % CI for the treatment difference had to be > -25 %, to demonstrate that the effectiveness of benralizumab was non-inferior to the effectiveness of mepolizumab. Secondary outcomes were not adjusted for multiplicity or controlled for type I error.

Abbreviations: ACQ-6 = Asthma Control Questionnaire (6-item version); BVAS = Birmingham Vasculitis Activity Score; CI = confidence interval; EGPA = eosinophilic granulomatosis with polyangiitis; OCS = oral corticosteroid; OLE = open-label extension; SNOT-22 = Sino-Nasal Outcome Test (22-item questionnaire)

Note: All oral corticosteroid doses listed in the DAD refer to oral prednisolone or prednisone (or an equivalent dose of prednisolone or prednisone if an alternative corticosteroid was used).

[a]that is requiring an increase in investigator-initiated oral corticosteroid dose, initiation or increased dose of immunosuppressive therapy, or hospitalisation.

In the primary analysis (data cut-off: August 2023), when added to oral corticosteroids with or without immunosuppressants, benralizumab demonstrated non-inferiority to mepolizumab for the primary outcome, main remission; similar response rates were also observed for supportive remission. Annualised relapse rate was also similar between the two treatment groups. However, there was a marked difference between the benralizumab and mepolizumab groups for the effect on the average daily dose of oral corticosteroid use during weeks 48 to week 52; numerically higher proportions of patients in the benralizumab group also had reductions of 100 % and ≥ 50 % in their average daily dose of oral corticosteroids.[2, 10] see Table 2.2.

The efficacy results of the main remission primary outcome, and of those achieving ≥ 50 % reduction in oral corticosteroid dose, informed the cost-effectiveness model.

Table 2.2. Efficacy results for MANDARA in the FAS population (data cut-off: August 2023).[2, 10]

	Benralizumab (n=70)	**Mepolizumab (n=70)**
Primary outcome: Proportion of patients with main remission at both weeks 36 and 48		
No. of patients in remission, n (%)	40 (57 %)	40 (57 %)
Difference[a] in remission rate (95 % CI), p-value	1.2 % (-14.1 to 16.5), p=0.88[b]	
Oral corticosteroid dose ≤ 4 mg per day	42 (60 %)	41 (59 %)
BVAS = 0	58 (83 %)	59 (84 %)
Secondary outcome: average daily dose of oral corticosteroids[c] during week 48 through week 52.		
Difference between the groups, odds ratio (95 % CI)	1.38 (0.75 to 2.54)	
Secondary outcome: reduction from baseline in average daily dose of oral corticosteroids[c] during Week 48 through week 52.		
Patients with ≥ 50 % reduction, n (%)	59 (84 %)	52 (74 %)
Patients with 100 % reduction, n (%)	29 (41 %)	18 (26 %)
Secondary outcome: Annualised relapse rate (ARR)		
ARR	0.50	0.49
Rate ratio for benralizumab/mepolizumab (95 % CI)	1.03 (0.56 to 1.90)	

BVAS = Birmingham Vasculitis Activity Score; CI = confidence interval; FAS = full analysis set

[a] Differences were for benralizumab vs mepolizumab; a positive number indicates that benralizumab is favoured. These percentages were adjusted for differences in baseline factors.
[b] p-value used for superiority testing differences between the treatment groups; this p-value was not statistically significant.
[c] The oral glucocorticoid dose was calculated as the daily dose of prednisone or prednisolone, regardless of the reason for administration. For patients who withdrew from the trial before week 52, the daily dose of oral glucocorticoid in the previous 28 days was used to derive the mean daily dose and percentage decrease in dose from baseline during weeks 48 through 52. Patients who discontinued treatment before week 48 were considered to have not had a response in the analysis of the percentage reduction in oral glucocorticoid dose.

The efficacy of benralizumab and mepolizumab were similar at week 52 for other patient-reported secondary outcomes that assessed changes in asthma (ACQ-6) and sinonasal (SNOT-22) symptoms from baseline.[2]

Of the 140 patients that were randomised to MANDARA 136 patients completed the 52-week double-blind treatment period, and 128 patients entered the ongoing open-label extension (OLE) period; all patients were treated with open-label benralizumab. Baseline characteristics of those entering the OLE were similar to the double-blind period. At the interim analysis data cut-off (August 2024), in the benralizumab-benralizumab group (n=66) and mepolizumab-benralizumab group (n=62) respectively, 92 % and 94 % of patients completed at least one year of the OLE (that is week 104). At week 104, benralizumab was associated with durable responses in remission (more than 60 % with main remission and more than 73 % with supportive remission); the proportions achieving remission were similar in both groups.[11]

2.2. Health-related quality of life (HRQoL) outcomes

HRQoL was assessed using the SF-36 questionnaire, which assesses general health and quality of life, with questions on eight domains of health, including physical and social functioning (higher scores indicate better health). Overall, similar changes from baseline at week 52 were observed in the benralizumab and mepolizumab groups.[2] The SF-36 data were not used in the cost-effectiveness model.

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing benralizumab with SoC, the submitting company presented a Bucher indirect treatment comparison (ITC). Nine efficacy outcomes were assessed, two of which informed the cost-effectiveness analyses: proportion of participants in remission in both Week 36 and Week 48 (main remission definition) and annualised relapse rate. Further details are presented in Table 2.3.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Bucher ITC. An anchored MAIC was also conducted as a supplementary analysis, with adjustment variables selected based on expert ranked potential effect modifiers.
Population	Adult patients with non-severe, relapsing or refractory EGPA.
Comparators	Benralizumab plus SoC compared with SoC alone (oral corticosteroids with or without immunosuppressants).
Studies included	MANDARA[10] (benralizumab plus SoC versus mepolizumab plus SoC), MIRRA[12] (mepolizumab plus SoC versus SoC alone)
Outcomes	• Proportion of patients with main remission at both weeks 36 and 48. • Annualised relapse rate. • Average daily dose of oral corticosteroids during week 48 through week 52.

Results	The Bucher ITC showed that: • Adding benralizumab to SoC resulted in a statistically significant improvement in the proportion of participants in main remission at both Week 36 and Week 48, compared with SoC alone; the OR was 17.75 (95 % CI: 3.33 to 94.67). • Adding benralizumab to SoC resulted in a numerical reduction in the annualised relapse rate compared with SoC alone; the RR was 0.57 (95 % CI: 0.28 to 1.15). • Adding benralizumab to SoC reduced the average daily OCS dose during the last four weeks of the study (weeks 48 through 52) compared to SoC alone. The results of the MAIC were similar but had more uncertainty.

CI = confidence interval; EGPA = eosinophilic granulomatosis with polyangiitis; HR = hazard ratio; ITC = Indirect treatment comparison; MAIC = matching adjusted indirect comparison; OR = odds ratio; RR = rate ratio; SoC = standard of care

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

In the MANDARA study, benralizumab was compared with mepolizumab; mepolizumab is a licensed treatment option for this indication though is not a relevant comparator in Scotland. The company's ITC versus SoC (section 2.3) did not compare safety outcomes.

In the double-blind period, there were similar proportions of adverse events (AEs) between the benralizumab (n=70) and mepolizumab (n=70) groups (90 % versus 96 %); most AEs reported, including COVID-19, headache and arthralgia were mild or moderate in severity, with a very low number of AEs leading to discontinuation (0% versus 2.9%). Four serious AEs were reported in the benralizumab group, with no specific AE occurring more than once. No fatal events were reported during the double-blind period of the study.[2] Safety data from the OLE were broadly consistent with the double-blind period.[11]

It is noted that the licensed dose of benralizumab for this indication (30 mg every 4 weeks) is more frequent than the dose for severe asthma (30 mg every 4 weeks for three doses then 30 mg every 8 weeks). Despite this, the safety profile of benralizumab for the treatment of patients with EGPA was generally consistent with the known safety profile of benralizumab, and no new safety concerns were identified.[2]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- MANDARA was a randomised, double-blind, phase III study with stratification, and baseline characteristics were generally well-balanced between the treatment groups; this makes it likely that there is a low risk of bias and provides reassurance about the internal validity of the study.[2] The definition for remission in the study outcomes utilised the validated BVAS[13], whilst the oral corticosteroid tapering target of ≤ 4 mg per day is recommended by British Society for Rheumatology (BSR).[3]
- Benralizumab, when added to SoC, demonstrated non-inferiority to mepolizumab for the primary outcome. Similar response rates between the benralizumab and mepolizumab groups

were observed using the supportive remission definition. Consistent trends in efficacy were noted for all secondary outcomes, including those which reduced oral corticosteroids, this would be a clinically relevant benefit for patients with EGPA.[2]

4.2. Key uncertainties

- The comparator in the MANDARA study was mepolizumab; however, it is not currently used for EGPA in Scottish clinical practice. The Bucher ITC comparing benralizumab with SoC had some imbalances in baseline characteristics between the groups (for example absolute blood eosinophil count and immunosuppressant use), which may be partly explained by the MIRRA study being conducted 5 years prior to MANDARA, and confidence intervals were wide. However, the ITC and MAIC appear to have been well conducted overall, and the conclusion of improved efficacy for benralizumab plus SoC compared with SoC alone appears reasonable.
- The 52 week study duration introduces uncertainty regarding longer-term comparative effectiveness, including the durability of remission, relapse dynamics beyond one year, and the potential benefit of benralizumab on sustained reduction of OCS use (and associated reduction in AEs).[10] The OLE showed results that were consistent with the double-blind period.[11]
- In the MANDARA study just over 50% of patients in both treatment groups had inactive disease (BVAS=0) at randomisation. However, in clinical practice, benralizumab would likely be considered for those with active disease (BVAS > 0 and active eosinophilic respiratory manifestations like asthma and rhinosinusitis). Despite this, the benefits of benralizumab observed in MANDARA are considered to be applicable to these patients.[3] Also, for those who entered MANDARA already in remission (BVAS=0), maintaining remission in addition to achieving a reduction in corticosteroid dose can be considered clinically meaningful by preventing the long-term cumulative adverse effects from prolonged corticosteroid use.[8]
- The MANDARA study excluded patients with severe (organ- or life-threatening) EGPA and excluded patients who had prior treatment with cyclophosphamide and rituximab (treatments used to stabilise severe EGPA). Clinical experts consulted by SMC confirmed that benralizumab would not be used to treat an acute severe EGPA episode. The summary of product characteristics (SPC) notes that benralizumab has not been studied in this population.[1]

4.3. Clinical expert input

Clinical experts consulted by SMC considered that benralizumab filled an unmet need and represents a therapeutic advancement by reducing eosinophil levels and oral corticosteroid use.

4.4. Service implications

Clinical experts did not anticipate any major service implications and highlighted that benralizumab is already used in Scotland for severe eosinophilic asthma.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified patient group.

- We received a patient group submission from Vasculitis UK, which is a charitable incorporated organisation.

- Vasculitis UK has received 1 % pharmaceutical company funding in the past two years, with none from the submitting company.

- Patients with EGPA not only have asthma but also sinus and nose symptoms and may have other symptoms including rashes, nerve damage, bowel trouble and blood loss and heart problems, muscle and joint pain and fatigue. As EGPA is chronic and flareups and relapses are not uncommon the burden of the illness is high.

- Patients believe that available treatments are not always as effective as targeted therapy and many have concerns about side effects particularly with corticosteroids.

- In general patients consulted by the patient group who have experience of benralizumab had positive comments, saying it helped to control their EGPA and asthma meaning they have less chest infections and could taper their steroids. They referred to it as life-changing, as they have less hospital appointments, making it easier for them to lead a more normal life and go to work, the ability to work is important to patients.

- Families of patients on benralizumab consulted by the patient group report less stress, fewer crises and a renewed sense of hope. Patients consulted by the patient group did not report any disadvantages of benralizumab.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An overview of economic analysis is presented in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis
Time horizon	Lifetime (maximum 60 years) with a cycle length of 28 days (half-cycle correction applied).
Population	Adult patients with relapsing or refractory EGPA
Comparators	SoC, which is OCS with or without IS. The OCS used in the economics was prednisolone, which was assumed to be used by 86.2 % of patients. The three IS agents were methotrexate, azathioprine and mycophenolate mofetil, used by 17.5 %, 32.5 % and 14.8 % of patients respectively.
Model description	The model was a cohort, Markov state-transition model with 3 health states plus death. The 3 health states were remission, stable disease and relapse. All patients started off in the stable disease state. A sub-model split the stable disease state into refractory and non-refractory disease. A set proportion of patients were assumed to have refractory disease at baseline, matched to the proportion observed in the MANDARA study.[2, 10] This proportion remained fixed across the duration of the model for those

	in the SoC arm. A reduction in the proportion of patients with refractory disease was observed between baseline and week 52 in the MANDARA study, and this risk reduction was incorporated into the model for patients in the benralizumab arm. Another sub-model was also used to capture the effects of long-term OCS use. Those effects included chronic comorbidities (type II diabetes, cardiovascular disease and osteoporosis) and acute events (adrenal insufficiency, cataracts, glaucoma, peptic ulcer, pneumonia and renal impairment).
Clinical data	Clinical data informing the outcomes of patients receiving benralizumab came from the MANDARA study. Transition probabilities between the health states for patients receiving benralizumab were informed by the observed movements. The MANDARA study compared benralizuamb against mepolizumab, and so to inform the base case comparison between benralizumab and SoC, the submitting company conducted a Bucher ITC (see Section 2.3 for details). A supplementary MAIC was also conducted and used in scenario analysis. The Bucher ITC was used to inform two parameters – the odds ratio for achieving remission, and the relative risk of relapse. The transition probabilities for patients receiving benralizumab were adjusted based in those parameters to estimate the transition probabilities for patients receiving SoC. Various published literature sources were used to inform OCS dosage, the rates of complications of those receiving OCS, and state specific standardised mortality ratios.
Extrapolation	The transition probabilities in the model were held constant from 52 weeks onward, until the end of the model's time horizon. The modelled assumed that patients receiving benralizumab could reduce their OCS. A tapering discontinuation rate, based on the observed rate of OCS reduction in MANDARA was applied across years 1 and 2 of the model. A benralizumab discontinuation rate was applied across the duration of the model. Upon discontinuation of benralizumab patients lost all treatment benefits instantaneously. No treatment waning was included.
Quality of life	Quality of life data was collected as part of the MANDARA study using the SF-36 instrument. These data were mapped onto the EQ-5D instrument. However, the submitting company received clinical feedback indicating the resulting utility values did not capture the impact of refractory or relapsed disease. The base case utilised utility values estimated from an international cross-sectional study of patients with EGPA, and severity defined by the patients' treatment physician – The Adelphi DSP. As scenarios the company explored values estimated by vignette studies conducted amongst members of the UK population and EGPA patients. All of the estimated utilities were considered academic in confidence by the submitting company and so cannot be reported here.
Costs and resource use	Costs included medicines costs, disease management costs and adverse event costs.
PAS/contract price	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount of was offered on the list price.

6.2. Results

The use of benralizumab was associated with increased costs, but also better health outcomes (estimated at an additional 1.43 QALYs). The resulting incremental cost-effectiveness ratio (ICER) was £19,403.

6.3. Sensitivity analyses

To explore areas of uncertainty the submitting company conducted deterministic sensitivity analysis, probabilistic sensitivity analysis and scenario analysis. A selection of scenarios are presented in Table 6.2.

Table 6.2: Scenario analysis results for benralizumab vs SoC (inclusive of benralizumab PAS discount).

#	Parameter	Base case	Scenario	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
	Base case				1.43	£19,403
1	Relative efficacy of benralizumab versus SoC	Informed by the Bucher ITC	Informed by MAIC	***CiC***	1.45	£19,043
2	Annual discontinuation rate	Base case value – based on mid-point of several alternative sources (value AiC)	Higher value (value AiC)	***CiC***	1.24	£18,770
3	Proportion of patients in refractory sub-state within stable disease health state at baseline	Proportion matched to MANDARA study (value AiC)	Starting % reduced by 5 %	***CiC***	1.38	£19,983
4			Starting % increased by 5 %	***CiC***	1.47	£18,869
5	Risk reduction in the number of benralizumab patients with refractory disease at 1 year	Risk reduction of equal to that observed in MANDARA	No risk reduction	***CiC***	1.27	£21,754
6	Source for health state utilities	Adelphi DSP study	General population valuation from vignette study	***CiC***	2.77	£9,980
7			Patient valuation from vignette study	***CiC***	3.27	£8,474
8			MANDARA-derived utility scores	***CiC***	0.57	£48,240

Abbreviations: AiC = academic in confidence; CiC = commercial in confidence; Incr. = Incremental; ICER =incremental cost-effectiveness ratio; ITC = indirect treatment comparison; MAIC = matched adjusted indirect comparison; OCS = oral corticosteroids; QALY = quality-adjusted life year, SoC = standard of care

6.4. Key strengths

- Key strengths were the appropriate model structure and appropriate comparator.

6.5. Key uncertainties

- There was a discrepancy between the definition of remission used in the economic analysis (which was aligned with the MANDARA study, where OCS dose reduction to 4mg/day or less was required) and clinical practice where a less strict value may be used (e.g. dose reduction to 7.5 mg/day or less). This introduces some uncertainty into the economic results, although any bias introduced would be expected to artificially reduce the estimated cost-effectiveness of benralizumab.
- The economic analysis ran a sub-model to separate refractory and non-refractory patients who have stable disease (that is neither relapse nor remission). This approach was adopted due to insufficient data to be able to populate refractory and non-refractory disease states separately in the main model. Whilst this was acknowledged, it was also felt that the application of static proportions between the refractory and non-refractory sub-states across the majority of the model may have introduced bias.
- The utility values applied in the modelling were a further source of uncertainty. The company did not use data collected as part of the MANDARA study as they felt that the estimated values lacked face validity, particularly failing to capture the impact of relapsed and refractory disease. Feedback received from clinicians consulted by SMC corroborated the company's assertion that relapse and refractory disease are highly impactful on quality of life, but it was unclear which of the various sources best represented patient experience. Alternative estimates had a large impact upon the ICER (see Scenarios 6, 7 and 8, Table 6.2).

*Other data were also assessed but remain confidential.**

7. Conclusion

After considering all the available evidence, the Committee accepted benralizumab for use in NHSScotland.

8. Guidelines and Protocols

The British Society for Rheumatology published guidelines for the management of ANCA-associated vasculitis in 2025.[3]

The European League against Rheumatism (EULAR) published recommendations on the management of ANCA-associated vasculitis in 2016; updated in 2022.[8]

9. Additional Information

9.1. Product availability date

07 February 2025.

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
Benralizumab 30 mg/mL solution for injection pre-filled pen	**30 mg subcutaneously every 4 weeks; a decision to continue the therapy should be made at least annually**	**25,415**

Costs from BNF online on 26 March 2026. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with-PAS budget impact due to commercial-in-confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 07 May 2026.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC includes Scottish national contract prices in its decision-making. These contract prices are commercial-in-confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.