

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Appraisal consultation document

**Benralizumab for treating severe eosinophilic
asthma**

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using benralizumab in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the [committee papers](#)).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using benralizumab in the NHS in England.

For further details, see NICE's [guide to the processes of technology appraisal](#).

The key dates for this appraisal are:

Closing date for comments: TBC

Second appraisal committee meeting: TBC

Details of membership of the appraisal committee are given in section 6.

1 Recommendations

1.1 Benralizumab, as an add-on therapy, is recommended as an option for treating severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids and long-acting beta-agonists, only if:

- the blood eosinophil count has been recorded as 400 cells per microlitre or more in the past 12 months and
- the person has agreed to and followed the optimised standard treatment plan, and has had at least 3 asthma exacerbations in the past 12 months and
- mepolizumab is not a treatment option and
- the company provides benralizumab according to the commercial arrangement (see section 2)

1.2 At 12 months:

- stop benralizumab if the asthma has not responded adequately or
- continue benralizumab if the asthma has responded adequately and assess response each year.

An adequate response is defined as:

- a clinically meaningful reduction in the number of severe exacerbations needing systemic corticosteroids or
- a clinically significant reduction in continuous oral corticosteroid use while maintaining or improving asthma control.

1.3 This recommendation is not intended to affect treatment with benralizumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Severe asthma is usually treated with inhaled corticosteroids plus another drug, such as a long-acting beta-agonist. These may not work well enough for eosinophilic asthma, which is a type of severe asthma that can be difficult to control. Continuous oral corticosteroids may be needed to prevent exacerbations (asthma attacks) but they can cause long-term side effects. Some people are able to have mepolizumab or reslizumab, which are biological treatments (as is benralizumab). These help to control the asthma, and may allow the oral corticosteroids to be reduced.

Clinical trial results show that taking benralizumab plus standard treatment reduces exacerbations and the use of oral corticosteroids, compared with placebo. There are no trials directly comparing benralizumab, mepolizumab and reslizumab, and the relative clinical effectiveness of these treatments is not known. In an indirect comparison of benralizumab with mepolizumab, there was no difference in asthma exacerbations.

The wide mixed population proposed by the company of people with 300 or more eosinophils, 3 or more exacerbations in the previous year, and including people who are, and are not taking maintenance oral corticosteroids, was not suitable for considering the cost effectiveness of benralizumab compared with standard care. This population includes people with varying severity of asthma, for whom the absolute treatment-benefit and cost effectiveness of benralizumab will vary and some will have alternative treatment options available.

When standard care is the only treatment option (that is, for people with an eosinophil count between 300 to 400 cells per microlitre, who have had 3 exacerbations and who are not taking oral corticosteroids), benralizumab cannot be recommended because no evidence is presented for this specific group of people.

Compared with mepolizumab, when this is a treatment option, benralizumab is not cost effective and cannot be recommended as an alternative to mepolizumab.

Compared with reslizumab, when this is a treatment option, benralizumab is a cost-effective use of NHS resources. However, this group includes people who have had 4 or more exacerbations or are taking maintenance oral corticosteroids, and they would also be eligible for mepolizumab as an alternative treatment option. Benralizumab is therefore recommended as an option for treating severe asthma in people with an eosinophil count of 400 cells per microlitre or more, who have had at least 3 exacerbations in the past year, only if mepolizumab is not a treatment option.

2 Information about benralizumab

Marketing authorisation indication	Benralizumab (Fasenra, AstraZeneca) is indicated as 'add-on maintenance treatment in adult patients with severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus long-acting β -agonists.'
Dosage in the marketing authorisation	The recommended dosage is 30 mg every 4 weeks for the first 3 doses then every 8 weeks, given by subcutaneous injection using a pre-filled syringe.
Price	The list price is £1,955.0 per 30 mg pre-filled syringe (company submission). The company has a commercial arrangement (patient access scheme). This makes benralizumab 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 (section 6) considered evidence submitted by AstraZeneca and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

New treatment option

People with severe eosinophilic asthma will welcome a new treatment option that reduces the need for oral corticosteroids

- 3.1 Severe eosinophilic asthma that is inadequately controlled despite high-dose inhaled corticosteroids plus long-acting beta-agonists is a debilitating condition, with many distressing symptoms. Exacerbations can happen without warning, be life threatening, cause fear, and result in hospitalisation and intubation. People are often unable to work and may need help with day-to-day activities because of the symptoms. The patient expert explained that, for many people with severe eosinophilic asthma, it does not respond to standard treatment and more intensive treatments are needed to control symptoms and prevent exacerbations. The clinical experts explained that standard treatment for inadequately controlled severe eosinophilic asthma is oral corticosteroids. NICE guidance recommends biological treatments such as [mepolizumab](#) and [reslizumab](#), which the patient expert noted have been life-transforming for some people. However, there are specific eligibility criteria for these drugs and not all patients are eligible to have them. The patient expert noted that inhaled or oral corticosteroids are the main treatment for preventing exacerbations in uncontrolled asthma. When taken frequently or long-term these can cause major side effects including diabetes, glaucoma, weight gain, bone-density loss, raised blood pressure and mood swings. This has a significant impact on the lives of patients and their families, including the need for numerous additional drugs and hospital visits to monitor and treat the side effects. The patient expert noted that the potential to reduce or avoid oral corticosteroids, over and above improved control of asthma symptoms, is particularly important to patients. The committee concluded that people with severe eosinophilic asthma that is uncontrolled on standard treatment would welcome a new treatment option that reduces or avoids the use of oral corticosteroids.

Benralizumab could offer an easier method of administration compared with existing biological treatments

3.2 The clinical experts explained that benralizumab is given as a subcutaneous injection using a pre-filled syringe. The dosing schedule is more convenient compared with reslizumab and mepolizumab that are both given every 4 weeks, needing frequent hospital visits. The committee heard that some people who meet the eligibility criteria for mepolizumab and reslizumab choose to remain on standard care because of personal preferences. The first 3 doses of benralizumab are given once every 4 weeks, and then every 8 weeks. The clinical experts considered this convenience in administration to be potentially very beneficial for patients. The patient expert highlighted that benralizumab would be preferred by many patients because its mode of administration and dosing schedule involves less travel and fewer visits to specialist centres. The patient expert and the clinical experts confirmed that reduction in oral corticosteroid use and its associated complications would be valuable to patients and significantly improve their quality of life. The committee concluded that benralizumab potentially offers benefits compared with existing biological treatments, by reducing visits to hospital, which could be important for people with severe eosinophilic asthma.

Clinical management

Mepolizumab and reslizumab are relevant comparators for benralizumab

3.3 The clinical experts explained that treatment for asthma in clinical practice follows the NICE guideline on [diagnosis, monitoring and chronic asthma management](#) and the Global Initiative for Asthma [2017 guideline](#) (which includes the use of mepolizumab, reslizumab and omalizumab). Management of uncontrolled asthma uses a step-up approach in which the dose of inhaled corticosteroids is continuously increased, while another drug is also taken for maintenance treatment. If the asthma is still uncontrolled, then oral corticosteroids are added. Because long-term use of corticosteroids is associated with side effects, the guidelines state that

inhaled and oral corticosteroids should be used at the lowest doses at which asthma control is maintained, and other treatments should be considered to minimise the use of oral corticosteroids. Eosinophilic asthma is a subtype of asthma, with inflammatory cellular infiltration in the airway. It can be associated with allergy, higher risk of exacerbations, hospitalisation, dependency on oral corticosteroids and increased risk of dying. Biological treatments for people with severe eosinophilic asthma that is inadequately controlled, despite taking high-dose inhaled corticosteroids and long-acting beta-agonists, aim to both reduce the number and severity of exacerbations and reduce or avoid the use of oral corticosteroids. The committee heard that the uptake of mepolizumab and reslizumab is lower than expected. This is partly because patients referred to tertiary centres have their care optimised on current treatments, which may mean their asthma improves sufficiently not to need a biological treatment. Also, some patients prefer not to have biologics because the administration regimens of mepolizumab (4-weekly) and reslizumab (intravenous infusion) can be difficult to maintain for personal reasons, the treatment is potentially life-long, and there is no long-term evidence on their use. The committee concluded that mepolizumab and reslizumab are both relevant comparators but the uptake of these are low because the guidance on mepolizumab and reslizumab is in the process of being implemented.

Comparators

The choice of comparator depends on oral corticosteroid use, eosinophil count and the number of exacerbations

- 3.4 The committee noted that the clinical trials recruited people with 2 or more exacerbations in the previous year. It noted that the company proposed a sub-population of people with a blood eosinophil count of 300 cells per microlitre or more, who have had 3 or more exacerbations in the previous year or are taking maintenance oral corticosteroids. The company considered that this represents people with more severe eosinophilic

asthma, who they consider will get the most benefit from benralizumab. The committee agreed to consider this population but noted that it includes people with differing severity of asthma (defined by eosinophil level, baseline oral corticosteroid use and the number of exacerbations in the previous year). It therefore includes people who would be offered different treatment options in the NHS:

- people with a blood eosinophil count of 300 cells per microlitre or more, who have had at least 4 exacerbations in the previous 12 months or who are taking oral corticosteroids, can have mepolizumab (although some may choose standard of care)
- people with a blood eosinophil count of at least 400 cells per microlitre, who have had at least 3 exacerbations in the last 12 months, can have reslizumab (although some may choose standard of care)
- people with a blood eosinophil count of 300 to 400 cells per microlitre, who have had exactly 3 exacerbations in the previous 12 months and are not taking oral corticosteroids, who would be offered standard of care because they are not eligible for a biological treatment.

Clinical effectiveness

Benralizumab is more clinically effective than standard care in the clinical trial populations

3.5 The company's clinical evidence comes from 3 trials: SIROCCO, CALIMA and ZONDA. These are randomised-controlled trials comparing benralizumab with placebo in people with uncontrolled asthma, taking inhaled corticosteroids and a long-acting beta-agonist. SIROCCO and CALIMA included people who had 2 or more exacerbations in the previous year and a blood eosinophil count of 300 cells per microlitre or more. ZONDA included people who had 1 or more asthma exacerbations in the previous year and a blood eosinophil count of 150 cells per microlitre or more. The primary outcome in SIROCCO and CALIMA was annual asthma exacerbation rate, and in ZONDA it was the percentage reduction in oral corticosteroid dose from baseline. The committee noted

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that the pooled results of SIROCCO and CALIMA show that benralizumab reduces the annual rate of exacerbations by 43% compared with placebo (risk ratio [RR] 0.57, 95% confidence interval [CI] 0.47 to 0.69; $p < 0.0001$) in the intention-to-treat population. The results also suggest that benralizumab is more clinically effective in people with a blood eosinophil count of 300 cells per microlitre or more, or in people who had 3 or more exacerbations. In a pooled subgroup analysis of people with a blood eosinophil count of at least 300 cells per microlitre who had 3 or more exacerbations, benralizumab significantly reduced the annual asthma exacerbation rate by 53% compared with placebo (RR 0.47, 95% CI 0.32 to 0.67; $p < 0.001$). Results from the intention-to-treat analysis from ZONDA showed that benralizumab reduced the median final oral corticosteroid dose by 75% from baseline, compared with a reduction of 25% for placebo (median treatment difference 37.5%, 95% CI 20.8 to 50.0; $p < 0.001$). Although the pooled SIROCCO and CALIMA data showed that benralizumab reduced the annual exacerbation rate the committee noted that the absolute reduction depends on the baseline rate, which is related to the severity of the asthma before treatment began. For example, for the same relative reduction, people who have had 4 exacerbations will experience a greater numerical reduction in exacerbations than people who have had 2 exacerbations. The clinical experts also explained that treatment will be more effective in people who have a higher blood eosinophil count than those with a lower blood eosinophil count. The committee concluded that benralizumab is clinically effective as an addition to standard care in people with a blood eosinophil count of at least 300 cells per microlitre, who have had 3 or more exacerbations or are taking maintenance oral corticosteroids, but the size of the benefit would be greater for patients who have had more exacerbations with higher eosinophil counts.

The mixed population compared with standard care is not appropriate for the purposes of decision making

3.6 The committee considered the population of patients proposed by the company (that is, people with a blood eosinophil count of 300 cells per microlitre or more, who have had 3 or more exacerbations in the previous year or are taking maintenance oral corticosteroids). The committee noted that the clinical trials included people with 2 or more previous exacerbations, and that the company's population had excluded people with 2 exacerbations and only included people with more severe eosinophilic asthma (3 or more exacerbations) on the basis that people with more severe asthma would benefit more from benralizumab treatment. The committee noted that the absolute effectiveness of benralizumab will be greater in people with more severe disease (that is, those who have had more exacerbations and/or with a higher eosinophil count). It noted that the range of asthma severity in the company's proposed population based on the pivotal trials may not be generalisable to people who have benralizumab in clinical practice in England. It considered this to be a key area of uncertainty, which will have a large impact on the clinical and cost effectiveness of benralizumab in any 'mixed' population. The committee was particularly interested in the proportion of patients with exactly 3 exacerbations, (including those with an eosinophil count between 300-400, who are not eligible for treatment with a biological treatment). It noted that the company's estimate on the proportion of people with exactly 3 exacerbations in response to the ACD was based on observational data (academic in confidence), and was higher than the proportion in the trials that was used in the economic model (also academic in confidence). This cast further doubt on the generalisability of the proposed population. The committee concluded that the mixed population proposed by the company, based entirely on the patient mix included in the trials is not appropriate for decision-making. Firstly standard of care is not the only comparator for this mixed population as some people would be eligible for other biologicals. In addition, there is major doubt about its generalisability to the NHS in

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England. The committee concluded that the mixed population was not suitable for the purposes of decision making. It is more appropriate to consider the clinical and cost effectiveness of benralizumab in relation to the severity of disease defined by oral corticosteroid use, eosinophil count and the number of exacerbations, and to take into account whether the patient was eligible for treatments other than standard care alone.

The clinical effectiveness of benralizumab compared with reslizumab and mepolizumab is uncertain

3.7 The committee noted that the company did not do a network meta-analysis (NMA) to compare the clinical effectiveness of benralizumab with reslizumab and mepolizumab, because of the significant differences in the patient populations in the trials for these 3 drugs. The company argued that it was more appropriate to adjust for differences in patient characteristics between the trials with an anchored matched-adjusted indirect comparison (MAIC), than an NMA. However, this was only feasible for the comparison with mepolizumab because differences in the baseline characteristics of the people in the reslizumab trial prevented a MAIC being done. Instead, the company assumed that benralizumab and reslizumab have the same clinical efficacy. The ERG agreed that a MAIC comparing benralizumab with reslizumab is not feasible, but it noted that there is no evidence to support the assumption of clinical equivalence. The committee agreed that no evidence had been provided to support this assumption and it concluded that the relative efficacy of benralizumab and reslizumab could not be determined. The committee noted that the MAIC with mepolizumab showed no significant differences between benralizumab and mepolizumab. However, a non-significant advantage of one over the other was shown, depending on whether data from the MUSCA trial were included in the analysis. MUSCA was a 24-week trial that was not included in the MAIC by the company because the primary outcome was health-related quality of life. Without the MUSCA data, the results favoured benralizumab but the reverse was the case if MUSCA data were included. The committee further noted that the MAIC comparing

benralizumab with mepolizumab was done in the full trial populations, because relevant subgroup data were not available for mepolizumab. The relative effect was assumed to apply to the subgroup of people with a blood eosinophil count of 300 cells per microlitre or more, who had 4 or more exacerbations. The committee heard from the company that the MAIC matched benralizumab patients to those in the mepolizumab trial and assumed that the relative difference in efficacy between the 2 treatments to be the same in the most severe subgroup as in the intention-to-treat population. The committee considered that despite the rationale provided during consultation, the use of the MAIC instead of an NMA had not been adequately justified. It also considered that the rationale is inconsistent with the company's use of the clinical-effectiveness estimates from the MAIC, which were applied to a population with different characteristics. The committee noted that a network meta-analysis of mepolizumab and reslizumab could have been done, and this might have been useful for its decision-making. However, it noted that a network meta-analysis may be affected by heterogeneity in the characteristics of the trial populations. The committee therefore concluded that there remains uncertainty about the clinical effectiveness of benralizumab compared with mepolizumab and reslizumab because the method used for the comparison with mepolizumab is not considered robust and a simple assumption of equivalence, with no underpinning evidence was used for reslizumab.

The company's economic model

The model structure is appropriate for decision making

- 3.8 The company submitted a 4-state Markov model comparing benralizumab with mepolizumab, reslizumab and standard care in people with a blood eosinophil count of at least 300 cells per microlitre, who had had 3 or more exacerbations or were taking maintenance oral corticosteroids. The committee noted that assessment of response was modelled at 52 weeks, when 'responders' continued taking the biological treatments and 'non-

responders' started standard care. The committee noted that the model included a stopping rule but were unclear if response was reassessed every year. The committee considered treatment continuation based on annual reassessment to be appropriate because, people have their asthma reassessed every year in clinical practice and was consistent with the reslizumab guidance (TA 479). The efficacy and clinical parameters in the model were derived from pooled SIROCCO and CALIMA data, ZONDA data, the MAIC results for the comparison of benralizumab with mepolizumab, published literature and previous NICE appraisals. The committee noted that the clinical effectiveness of benralizumab compared with mepolizumab was based on a MAIC, which it had considerable reservations about (see section 3.7). However, the committee considered it commendable that the model attempted to incorporate some of the long-term complications of oral corticosteroid use in the model, even though some effects cannot be reversed so some steroid-sparing benefits may not be realised. Taking everything into account, the committee accepted that the model structure is appropriate for decision making.

Clinical inputs to the model

There is considerable uncertainty about the proportion of people taking maintenance oral corticosteroids at baseline in the comparison with mepolizumab and standard care

3.9 In response to consultation the company provided an updated model, which included an updated confidential discount to the list price of benralizumab and updated many of the model inputs to those preferred by the committee. Different proportions of maintenance oral-corticosteroid use at baseline were used, depending on the comparator (54.1% for standard care and 60% for mepolizumab). The ERG preferred a value of 41.7%, sourced from a UK registry of patients with severe asthma (Heaney 2010) for the standard care comparison and 60% for the mepolizumab comparison. The clinical experts confirmed that in clinical practice in the UK, about 66% to 80% of people starting to take

mepolizumab will be taking maintenance oral corticosteroids. The committee noted that it is difficult to determine the proportion of people taking maintenance oral corticosteroids in the company's mixed population (see section 3.6). This is a key area of uncertainty in the model, which has a substantial impact on the cost effectiveness of benralizumab.

The amended asthma-related mortality estimates are appropriate

3.10 The committee noted that asthma-related mortality is often a key driver of cost effectiveness in asthma models. It heard from the clinical experts that the National Review of Asthma Deaths (NRAD) report indicated that asthma-related deaths have decreased substantially in all age categories, except in people over 75. The clinical experts explained that asthma-related deaths are rare, with about 300 to 400 deaths annually in the UK. They commented that some deaths originally recorded as asthma-related in the NRAD report were later found not to have been caused by asthma. The committee noted that in the model provided by the company in response to the first appraisal consultation document, asthma-related mortality was updated to include an average probability of death of 0.0078 per hospital admission (sourced from the British Thoracic Society asthma audit for people aged 45-54 years and 55-64 years). This was preferred by the committee. The committee concluded that the asthma-related mortality estimates in the company's revised model are appropriate.

The company's updated base-case economic analysis

The company's mixed asthma severity population is not suitable for making decisions about the cost effectiveness of benralizumab with standard care

3.11 The committee considered the mixed population proposed by the company of people with a blood eosinophil count of at least 300 cells per microlitre, who had had 3 or more exacerbations or were taking maintenance oral corticosteroids. The modelled population requires assumptions to be made about the proportion of patients on maintenance oral corticosteroids, the proportion of patients by number of prior

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exacerbations, and by level of blood eosinophil count who would be considered for this treatment in clinical practice. It noted that there is considerable uncertainty associated with the generalisability of severity of asthma in this population to clinical practice in England (see section 3.6). It noted the significant effect on clinical effectiveness of severity of disease (defined by oral corticosteroid use, eosinophil count and number of exacerbations) which will also affect the cost-effectiveness results. The committee noted that within this population some people would be eligible for treatment with other biologics, and were therefore only interested in the ICER compared with standard care in people who were not eligible for biologics which was not provided. The committee concluded that the base-case deterministic ICER in the mixed population for benralizumab compared with standard care provided by the company in response to consultation (£29,896 per QALY gained) and the ERG exploratory analysis (£32,179 per QALY gained) were not relevant to decision-making. It noted ERG exploratory subgroup analyses in people who had 3 or more exacerbations and who are not taking maintenance oral corticosteroids resulted in an ICER of £40,379 per QALY gained. For these reasons, the committee did not consider it appropriate to base its decision-making on the ICER from a mixed severity population based solely on proportions from the trials.

Cost-effectiveness estimates

When mepolizumab is an appropriate treatment option (people who have an eosinophil count of at least 300 cells per microlitre and have had 4 or more exacerbations or who are taking oral corticosteroids), the ICER is above the range normally considered a cost-effective use of NHS resources

3.12 The committee considered the population of people who are taking oral corticosteroids or have had 4 or more exacerbations with an eosinophil count of at least 300 cells per microlitre. Taking into consideration the PAS prices for benralizumab and mepolizumab, the committee noted that benralizumab was clearly not cost effective. The committee acknowledged

that there is some benefit for benralizumab, particularly in the method and frequency of administration. However it noted that the QALY gain for benralizumab in the company's model is small and based on an assumption of superior clinical benefit for benralizumab from the MAIC, which the committee did not accept as robust (see section 3.7). The committee concluded that even if it accepted the improved efficacy of benralizumab compared with mepolizumab in the MAIC, it is not cost effective compared with mepolizumab.

When reslizumab is an appropriate treatment option (people who have an eosinophil count of at least 400 cells per microliter and have had at least 3 exacerbations, the ICER for benralizumab is within the range normally considered to be a cost-effective use of NHS resources

3.13 The committee considered the population of people who have an eosinophil count of at least 400 cells per microlitre and have had at least 3 exacerbations. It noted that when the PAS prices for benralizumab and reslizumab were taken into consideration in the ERG analysis, benralizumab is clearly cost effective compared with reslizumab. It considered that although the simple assumption of clinical equivalence between the 2 treatments is questionable, it is reasonable to assume that they are not very different. The committee was sufficiently reassured that the ICERs are robust to small differences in the clinical effectiveness. It concluded that benralizumab can be considered cost effective in people who are eligible for reslizumab. It acknowledged the benefit of benralizumab, particularly in the method and frequency of administration compared to the intravenous administration or reslizumab. However, the committee noted that some patients eligible for reslizumab will also be eligible for mepolizumab if they had 4 exacerbations in the past year or are taking oral corticosteroids. Benralizumab is not cost effective compared with mepolizumab, so cannot be recommended in those for whom mepolizumab is a treatment option.

When standard care is the only treatment option, benralizumab is not a cost-effective use of NHS resources

3.14 The committee considered the population for whom standard care is the only treatment option (people with an eosinophil count between 300 to 400 cells per microlitre, who have had 3 exacerbations and who are not taking oral corticosteroids). It heard from the clinical experts that many people with inadequately controlled eosinophilic asthma who are not eligible for treatment with biologics would in clinical practice receive oral corticosteroids instead of continuing on inhaled medication alone. The committee noted that the company proposed the use of benralizumab earlier in the treatment pathway than where other biological treatments are currently used and would therefore need to be convinced of the clinical and cost effectiveness of benralizumab in this specific population. The company did not provide the ICER for this population but the committee considered the ERG's exploratory analysis of the company's mixed population, in which no patients were taking oral corticosteroids (which would have included some patients with 300 to 400 eosinophils per microlitre and only 3 exacerbations). This resulted in an ICER of £40,379 per QALY gained, which it considered to be an underestimate because it was calculated for a population including people with more severe disease. The committee concluded that benralizumab is not cost-effective for treating severe eosinophilic asthma in people who are not taking oral corticosteroids, have had 3 exacerbations and with an eosinophil count between 300 to 400 cells per microlitre.

Innovation

3.15 There are no additional benefits that are not captured in the QALY calculations.

3.16 The committee noted that benralizumab results in near-complete depletion of blood eosinophils within 24 hours of the first dose, and this depletion is maintained throughout the treatment period. Mepolizumab and reslizumab indirectly reduce the activation, proliferation, and survival

of eosinophils resulting in eosinophil reduction but not near-complete depletion. Complete loss of eosinophils could be beneficial, however it could theoretically carry some risks. The clinical experts commented that benralizumab is the only biologic treatment available as a pre-filled syringe, and that it has a more convenient 8-week dosing schedule. People are not currently able to self-administer benralizumab at home, but this might become possible in future. The clinical experts expressed the opinion that the differences in mode of action for benralizumab compared with mepolizumab and reslizumab are not of themselves innovative, but the convenience of administration of benralizumab would ease some of the burden of living with severe eosinophilic asthma. The committee concluded that benralizumab would be beneficial for patients, but it had not been presented with evidence that there are additional benefits that had not been captured in the cost-effectiveness analyses.

4 Implementation

- 4.1 Section 7(6) 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 eosinophilic asthma and the doctor

responsible for their care thinks that benralizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Proposed date for review of guidance

5.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Jane Adam

Chair, appraisal committee

July 2018

6 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 A](#).

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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