NICE National Institute for Health and Care Excellence

NICE guidance

Reslizumab for treating severe eosinophilic asthma

Technology appraisal guidance
Published: 4 October 2017

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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 Reslizumab, as an add-on therapy, is recommended as an option for the treatment of severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids plus another drug, only if:

- the blood eosinophil count has been recorded as 400 cells per microlitre or more
- the person has had 3 or more severe asthma exacerbations needing systemic corticosteroids in the past 12 months and
- the company provides reslizumab with the discount agreed in the patient access scheme.

1.2 At 12 months:

- stop reslizumab if the asthma has not responded adequately or
- continue reslizumab 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 These recommendations are not intended to affect treatment with reslizumab that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations 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.

2 The technology

Table 1 Summary of reslizumab

Description of the technology	Reslizumab (Cinqaero, Teva) is an interleukin-5 inhibitor that reduces eosinophil numbers and activity.
Marketing authorisation	Reslizumab has a marketing authorisation in the UK as 'add-on therapy in adult patients with severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus another medicinal product for maintenance treatment'.
Adverse reactions	The most common adverse reaction is increased blood creatine phosphokinase, which is transient and asymptomatic. For full details of adverse reactions and contraindications, see the summary of product characteristics.
Recommended dose and schedule	Intravenous infusion based on body weight once every 4 weeks. For patients between 35 kg and 199 kg the recommended dose is achieved using a vial-based dosing scheme. For patients below 35 kg or above 199 kg the recommended dose is 3 mg/kg body weight.
Price	The list price is £499.99 per 100-mg vial and £124.99 per 25-mg vial (excluding VAT). The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of reslizumab, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

3 Evidence

The appraisal committee considered evidence submitted by Teva and a review of this submission by the evidence review group. See the committee papers for full details of the evidence.

4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of reslizumab, having considered evidence on the nature of severe eosinophilic asthma and the value placed on the benefits of reslizumab by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

Patient experience

4.1 Inadequately controlled severe eosinophilic asthma is a distressing and socially isolating condition. The committee heard from the patient expert that severe asthma has an unpredictable course. People with very severe asthma are often unable to work and may need help with day-to-day activities because of the symptoms. Exacerbations are very frightening and can happen without warning. They can result in frequent hospital visits and in severe cases are life-threatening, which may require intensive care support including intubation. The committee heard from the clinical experts that standard treatment for inadequately controlled severe eosinophilic asthma is corticosteroids. These are often effective, and oral or injected corticosteroids are the mainstay of treatment for exacerbations, but when taken frequently or long term they are associated with some major complications. The patient expert explained that these include diabetes, glaucoma, weight gain, bone density loss, hip replacement, raised blood pressure and mood swings. These can have a significant effect on patients, and can mean that numerous additional medications are needed to counteract the effects of the corticosteroids. The committee heard from the patient expert that she has to attend appointments for these complications, and it takes between 2 and 4 hours daily to administer all of her medicines. The committee understood that people would welcome treatment options that replace the need for, or reduce the dose of, oral corticosteroids. The committee heard that treatments such as reslizumab reduce the number of exacerbations, and are also expected to reduce oral corticosteroid use. It concluded that inadequately controlled severe eosinophilic asthma is associated with substantial morbidity and that there is a need for alternative treatment options.

Current clinical management of asthma

4.2 The clinical experts explained that treatment for asthma in clinical practice follows guidelines from the British Thoracic Society and the Scottish Intercollegiate Guidelines Network. The clinical experts explained that the management of severe eosinophilic asthma lies within what were previously known as step 4 and step 5 of the superseded 2014 version of these guidelines. The current guidelines (2016) suggest that people having high-dose inhaled therapies (previously step 4) or continuous or frequent use of oral corticosteroids (previously step 5) should be referred for specialist care. Additional interventions may include leukotriene receptor antagonists, theophyllines, oral corticosteroids, and help with smoking cessation. The committee understood that oral or injected corticosteroids can be used for short periods, for example to manage an exacerbation, but oral corticosteroids can be used as long-term maintenance. The committee was aware that the marketing authorisation for reslizumab is for 'severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus another medicinal product for maintenance treatment'. It questioned whether only people who continue to have exacerbations despite treatment with continuous or frequent use of oral corticosteroids (previously step 5 of the guidelines) would be eligible for reslizumab. The clinical experts explained that people who have severe uncontrolled eosinophilic asthma having high-dose therapies (previously step 4) or continuous and frequent use of oral corticosteroids (previously step 5) would have treatment at specialist centres, and that many of these patients have asthma that will respond to optimised treatment. Reslizumab would only be considered for patients who continue to have clinically significant exacerbations despite optimised conventional treatment, and about 50% of these people might be taking maintenance oral corticosteroids. The committee understood that people with severe eosinophilic asthma on optimised treatment described in the high-dose therapies (previously step 4) or continuous and frequent use of oral corticosteroids (previously step 5) stages of the guidelines would be considered eligible for treatment with reslizumab.

Diagnosing severe eosinophilic asthma

4.3 The clinical experts explained that there are no standard diagnostic criteria for

severe eosinophilic asthma in clinical practice. The committee heard that clinicians use the patient's phenotype to come to a probable diagnosis, which is confirmed using objective criteria in the form of evidence of eosinophilia (including blood or sputum eosinophil counts, exhaled nitric oxide levels, or biopsy specimens from nasal polyps). A rapid response to oral corticosteroids is also used to diagnose eosinophilic asthma. The committee heard that peripheral blood eosinophil count is a commonly used biomarker but it is suppressed by corticosteroid use, therefore only measurements taken before corticosteroid treatment are reliable. The clinical experts stated that measuring sputum eosinophils gives the most accurate diagnosis of eosinophilic asthma, but this is not widely used in clinical practice. The committee acknowledged the complexity of diagnosing eosinophilic asthma.

Clinical effectiveness

Population

4.4 The committee discussed the generalisability of the clinical trials to UK clinical practice. The company presented evidence from trials that included people aged 12 to 75 years with asthma and a blood eosinophil count of 400 cells per microlitre or more, inadequately controlled with medium to high-dose inhaled corticosteroids. The committee noted that the key trials, study 3082 and study 3083, included people with a blood eosinophil count of more than 400 cells per microlitre in the previous 12 months. The committee was aware that the marketing authorisation for reslizumab does not give a specific eosinophil count because the European Medicines Agency stated that blood eosinophil levels are not sufficiently predictive to include a cut-off value. The clinical experts stated that the high eosinophil count threshold was a limitation of the clinical trials because reslizumab is more effective the higher the eosinophil count, and therefore it might not be as effective in clinical practice as in the trials. They also explained that some patients in the trials may have had sensitivity to fungal allergens, which would account for the high eosinophil counts seen at baseline. However, the clinical experts clarified that people with lower eosinophil counts than those in the trials may also potentially benefit from treatment with reslizumab. The committee noted that a small proportion of patients in the trials

were taking oral corticosteroids, but they were not permitted to reduce their corticosteroid dose during the trial. The committee concluded that the studies are relevant to the UK but that, in clinical practice, patients considered for this treatment may have lower eosinophil counts than in the trials and a higher percentage will be on oral corticosteroids.

Frequency of exacerbations

4.5 The committee noted that study 3082 and study 3083 recruited people with 1 or more exacerbations in the previous year. It was aware that the company proposed, and presented a base-case cost-effectiveness analysis for, a restricted population including people with 3 or more exacerbations per year. The committee heard from the clinical experts that they would particularly like to have this treatment available for patients having maintenance oral corticosteroids who have 3 or more exacerbations per year. The committee also heard that the number of exacerbations in 1 year does not necessarily indicate future exacerbation rates, and that event rates vary in patients from year to year. It considered that this is a limitation of the trials, which looked at only 1 year in what is a variable and lifelong condition. However, the committee noted a comment from a consultee in response to the second consultation that previous exacerbations are a strong predictor of subsequent exacerbations. The committee concluded that a criterion based on the number of exacerbations was not unreasonable, and expressed the view that the more frequent the exacerbations, the greater the clinical need.

4.6 The committee discussed whether treatment with reslizumab would be appropriate for people who do not take maintenance oral corticosteroids. The clinical experts highlighted that probably at least 50% of patients on what were previously known as steps 4 or 5 of the British Thoracic Society and Scottish Intercollegiate Guidelines Network guidelines are having treatment with maintenance oral corticosteroids, but still have several exacerbations. The clinical experts explained that these people would be eligible for treatment with reslizumab but there are also other patients, who are not taking maintenance oral corticosteroids, who would benefit from reslizumab treatment. Patients who are not taking maintenance oral corticosteroids may have 1 of the following maintenance treatments in addition to high-dose inhaled corticosteroids:

leukotriene receptor antagonists, theophylline, slow-release beta-2 agonists or tiotropium. The committee considered the clinical experts' statements that maintenance corticosteroids are an effective treatment for people with severe asthma, and that a proportion of people who are taking maintenance corticosteroids will still have uncontrolled severe eosinophilic asthma. The committee noted that there are limited data on the effectiveness of reslizumab in people who are on maintenance corticosteroids, because only 19% and 12% of people respectively in study 3082 and study 3083 fulfilled this criterion. The committee concluded that reslizumab may be considered for people who are not taking maintenance oral corticosteroids, but it would be most beneficial for people who have multiple exacerbations despite maintenance oral corticosteroid use.

Comparison with mepolizumab

4.7 The committee noted that at its first meeting, and in response to the first consultation, comparison with NICE's technology appraisal guidance on mepolizumab was raised as an issue. Several consultees stated the desirability of a recommendation that is the same for reslizumab and mepolizumab in terms of eosinophil count, number of exacerbations and oral corticosteroid usage. The committee noted that mepolizumab was not in the NICE scope as a comparator for this appraisal, and therefore no comparative data had been presented by the company. The committee acknowledged that clinicians might want to use reslizumab and mepolizumab interchangeably in clinical practice. However the company submission was based on the trial data for reslizumab, which differs from the evidence base for mepolizumab. The committee therefore had no information on the clinical and cost effectiveness of reslizumab in a population similar to that in the NICE guidance for mepolizumab; that is, people with an eosinophil count of 300 cells per microlitre, 4 or more exacerbations in a year, or taking continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months. The committee concluded that it could only consider the data presented by the company, and it had no information that allowed it to make a recommendation for reslizumab in line with mepolizumab.

Direct comparison with best supportive care

4.8 The committee considered the results from the trials, including study 3082 and study 3083. It noted that reslizumab, compared with placebo, was associated with lower rates of clinically significant exacerbations. The committee concluded that, compared with placebo, reslizumab is effective in reducing the rate of clinically significant exacerbations.

Indirect treatment comparison with omalizumab

4.9 The committee noted that the NICE scope included omalizumab as a comparator in a small 'overlap' population of people who also had severe persistent allergic IgE-mediated asthma, and therefore could have either reslizumab or omalizumab. It heard that clinicians would decide which drug is most appropriate based on the person's phenotype. For predominantly eosinophilic symptoms, such as nasal polyps and sinusitis, people would be offered reslizumab. However, the committee noted the comment from a consultee in response to the second consultation that reslizumab may not be more appropriate than omalizumab for this group. People with predominantly IgE-related symptoms, such as eczema and urticaria, would be offered omalizumab. The committee noted that the company had presented an indirect treatment comparison using data from study 3082 and study 3083 for reslizumab and from the INNOVATE and EXTRA trials for omalizumab. It noted that the company based its comparison on the full trial populations, but there are fundamental differences between them. The committee acknowledged that the 2 drugs have different mechanisms of action and different populations. It also considered that adjusting for these differences in the very small overlap population was unlikely to be robust. The committee concluded that the results from the company's indirect comparison of reslizumab with omalizumab were highly uncertain and not suitable for decision-making. The committee therefore did not consider this comparison further.

Cost effectiveness

4.10 The committee considered the company's cost-effectiveness analysis. It noted that the company's original base case was for reslizumab compared with

standard care, for people with severe asthma who have had 3 or more exacerbations in the previous year. The committee noted that this is a subgroup of the overall trial population of people with severe asthma who have had 1 or more exacerbations in the previous year. The committee recalled its previous conclusion (see section 4.4) that neither the trials, nor the base-case populations, accurately reflect patients in the UK who might be considered for reslizumab; people with severe disease despite optimised care, often with lower eosinophil counts than in the trials, and with higher rates of maintenance corticosteroid use. The committee noted that the company had also presented cost-effectiveness analyses comparing reslizumab with omalizumab. The committee recalled its previous conclusion (see section 4.9) that the comparison with omalizumab is highly uncertain and not suitable for decision-making. The committee concluded that it would only consider the company's analysis for reslizumab compared with best standard care using the results from study 3082 and study 3083.

Choice of standard care

4.11 The committee discussed the choice of standard care in the company's model. The committee was aware that the model did not incorporate stopping or reducing the dose of oral corticosteroids, because oral corticosteroid dose had been kept constant in the trials. It queried whether standard care with long-term maintenance oral corticosteroids is a more appropriate comparator than standard care with oral corticosteroids taken in short courses. The committee recalled the evidence from the clinical experts that 50% of patients with severe eosinophilic asthma may already be on maintenance oral corticosteroids. The clinical and patient experts stated that the long-term effects of oral corticosteroid treatment are serious and could become as problematic as the asthma itself (see section 4.1). The clinical experts stated that some observational data exist on oral corticosteroid sparing and the costs associated with treating corticosteroid-induced complications. The committee noted that in response to the appraisal consultation documents the company had discussed the issues around oral corticosteroid sparing, but the model structure did not allow the costs and consequences of oral corticosteroid use to be incorporated. The committee agreed it would have liked to have seen some exploratory analysis around this issue to explore the potential benefit of reslizumab in reducing oral corticosteroid

use and therefore the adverse effects associated with oral corticosteroids, as suggested by the clinical experts (see section 4.1). The committee also noted a comment received in response to consultation that there was an ongoing corticosteroid reduction trial. The committee heard from the company that a trial of a subcutaneous formulation of reslizumab, that examined the effect of oral corticosteroid sparing, had been requested by the regulators and was underway. The committee concluded that because more patients in UK clinical practice have maintenance oral corticosteroids than those in the trials, this potential benefit of reslizumab had not been taken into account in the cost-effectiveness analysis. It expressed interest in evidence in support of this proposed benefit when further trial data become available.

Exacerbation transition probabilities

4.12 The committee considered the company's approach to estimating transition probabilities between exacerbation states of the economic model. In the original base case the company had noted that patients randomised to placebo, as well as those in the reslizumab arm of the trials, experienced a reduction in exacerbations. The company stated that this reflects a potential placebo effect. To account for this placebo effect, the company adjusted the estimates in both the placebo and the reslizumab arms. The committee heard from the clinical experts that patients in both arms of the trials would be carefully followed and monitored during the trial, so would have had optimised, closely supervised care, which they may not have had before entering the trial. This could account for at least some of the improvement, rather than it being a placebo effect. The committee agreed that improvement could reflect the benefit of optimised care, or regression to the mean. This would be likely to affect both arms, and the adjusted rates were no more likely than the unadjusted rates to reflect the true treatment benefit of reslizumab. The committee agreed that it would have preferred to see results from a model that used the observed (unadjusted) data from the relevant subgroup in the trials to determine the transition probabilities. In response to the second appraisal consultation document, the company provided a revised base-case analysis that did not include an upward adjustment in the exacerbation rate of the standard care arm, so closely reflected the actual baseline exacerbation rate seen in the trials. Transition probabilities used in the model submitted in response to the first appraisal document, but without the

placebo adjustment, were incorporated in the company's revised base case. Based on these updated transition probabilities, the model used a mean annual exacerbation rate of 2.68 for standard care (instead of the previous value of 4.85) which the committee accepted was slightly lower than the mean rate of exacerbation of 2.73 reported in the placebo arms in the clinical trials. The committee concluded that this approach was in line with their original request and that the revised analysis was appropriate.

4.13 In response to consultation, the company highlighted that using the baseline exacerbation rate seen in the trials was likely to be conservative. It highlighted several UK studies that showed severe asthma patients attending specialised centres have a higher level of exacerbations than in their revised model. In response to the committee's previous concern around whether the higher rate of 4.85 exacerbations would apply to people with severe eosinophilic asthma, the company reported new evidence showing that patients with severe eosinophilic asthma had roughly similar exacerbation rates to patients with non-eosinophilic asthma (although it acknowledged that the results lacked statistical significance). The company further explored this expected higher rate in a scenario analysis. This was based on the approach suggested by the evidence review group (ERG) in their previous report, in which the observed rate of exacerbation in the clinical trial (2.68) was assumed to apply for the duration of the trial (that is 1 year) and was then assumed to increase linearly over the following 9 years until the exacerbation rate of the 'real world' data (that is 4.85 exacerbations per year) was reached at year 10. The committee noted the company's evidence supporting higher exacerbation rates than seen in the clinical trials, but concluded that the most robust estimate of relative effectiveness was derived from the exacerbation rates shown in the clinical trials, and that this was the best available data for decision-making.

Duration of treatment

4.14 The committee discussed the duration of treatment with reslizumab assumed by the company in its model. The committee noted the company's algorithm that calculated the expected response at the end of the year based on an early response at 16 weeks. The clinical experts stated that patients would not routinely be assessed for response to reslizumab at 16 weeks because this is too

early to assess the effect on exacerbations, and other measures would not be reliable enough. A more appropriate reassessment period would be 6 months, followed by annual reassessments. The clinical experts stated that if patients continued to benefit from treatment, they would remain on reslizumab indefinitely. In response to consultation the company showed that there is minimal difference in cost effectiveness for reassessment at 16 weeks, 6 months or 52 weeks. The committee also noted other consultation comments that patients on other asthma drugs are reassessed at 16 weeks and therefore it would be helpful to use this same reassessment time point for reslizumab. However, the committee noted a response to the second consultation that suggested 16 weeks was not appropriate for reslizumab and perhaps, given that reslizumab has the same mechanism of action as mepolizumab, a reassessment at 12 months would be more appropriate. The committee heard from the company that no rule for stopping treatment with reslizumab was incorporated in the economic model. But the company clarified that a proportion of patients were modelled to stop treatment at 16 weeks because of early response, and at 52 weeks for lack of clinical response, and that the summary of product characteristics for reslizumab says treatment should be reassessed at 12 months. The committee therefore concluded that reassessment at 12 months was the most appropriate.

Administration costs and drug wastage

4.15 The committee considered the administration costs used by the company in its model. The committee noted that in its response to the first consultation, the company updated the administration costs to reflect clinical practice. The committee concluded that the company had included more appropriate administration costs for reslizumab in its revised model.

4.16 The committee noted that reslizumab has a marketing authorisation at a dose of 3 mg/kg given intravenously every 4 weeks, using a 100-mg vial and a 25-mg vial. It was aware that the company had submitted a change in the summary of product characteristics to incorporate vial-based dosing by bodyweight, which had been accepted. The committee heard from the company that vial-based dosing would simplify the dose determination process and reduce preparation time, minimise wastage and reduce the total cost of treatment. This is because

patients in each dosing group will have a dose slightly lower than the 3 mg/kg weight-based dosing. The company further highlighted that clinical response and efficacy would be maintained compared with weight-based dosing. The ERG considered this to be a reasonable approach and the committee concluded that vial-based dosing was appropriate.

Utility values

4.17 The committee discussed the estimates of utility in the model. The ERG's view was that the company's original base case should have used values mapped from AQLQ to EQ-5D, because the evidence came from the trials. In response to the first consultation, the company's revised base case used the ERG's preferred utility values. In response to the second consultation, the company updated the mean utility values for the severe exacerbation health state. Post-hoc analyses from the clinical trials showed that patients with severe eosinophilic asthma, with 3 or more exacerbations in the previous year, had a lower mean duration for a severe exacerbation in the reslizumab arm compared with the placebo arm. The committee noted that based on this information, the company changed the utility value of 0.51 for both reslizumab and best supportive care for the duration of the full model cycle (4 weeks) in the severe exacerbation state to 0.54 for reslizumab and 0.50 for best supportive care. The ERG highlighted the uncertainty in these utility value estimates because of the lack of robust health-related quality-of-life data, but considered the calculation to be appropriate. It further noted that the revised utility values had only a minor effect on the cost effectiveness. The committee therefore accepted the revised utility value estimates for severe exacerbations.

Incremental cost-effectiveness results

4.18 The company presented its revised base case, in response to consultation, taking into account the revised patient access scheme discount applied to reslizumab compared with best standard care. The company's base-case deterministic incremental cost-effectiveness ratio (ICER) for people with 3 or more exacerbations in the previous 12 months is £29,870 per quality-adjusted life year (QALY) gained and the probabilistic ICER for people with 3 or more exacerbations

in the previous 12 months is £27,509 per QALY gained. The committee again noted comments from consultees which highlighted the need to see the oral corticosteroid sparing effect of reslizumab being captured in the economic model. It was aware that there are limited data supporting the potential benefits of interleukin-5 inhibitors in reducing oral corticosteroids. The committee concluded that, had the potential benefits of oral corticosteroid sparing been included in the economic analysis, the most plausible ICER for reslizumab could be slightly lower and any future data on this would be welcomed. The committee agreed that reslizumab could be considered a cost-effective use of NHS resources and concluded that reslizumab, as an add-on therapy, could be recommended as an option for treating severe eosinophilic asthma that is inadequately controlled despite maintenance therapy with high-dose inhaled corticosteroids, only if the blood eosinophil count has been 400 cells per microlitre or more and the person has had 3 or more asthma exacerbations in the previous 12 months.

Pharmaceutical Price Regulation Scheme

4.19 The committee was aware of NICE's position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014, and in particular the PPRS payment mechanism. It accepted the conclusion 'that the 2014 PPRS payment mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines'. The committee heard nothing to suggest that there is any basis for taking a different view in this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

Innovation

4.20 The committee heard from stakeholders that reslizumab is innovative in its potential to make a significant and substantial effect on health-related benefits. The committee heard from the clinical experts that there are few treatments for severe eosinophilic asthma that have the potential to reduce corticosteroid use. It noted that it had not seen any evidence on preventing or delaying the use of

maintenance oral corticosteroids but heard from the clinicians that this is an important aim of treatment with reslizumab. The committee agreed that some benefits related to avoiding the significant adverse effects of oral corticosteroid use had not been fully captured in the QALY calculations. The committee also considered that there were benefits to carers, which may not have been captured in the QALY calculation. The committee therefore agreed that reslizumab could be considered innovative.

5 Implementation

5.1 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.

5.2 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 determination.

5.3 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 reslizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5.4 The Department of Health and Teva have agreed that reslizumab will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to general.enquiries@tevauk.com.

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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