NICE National Institute for Health and Care Excellence

NICE guidance

Mepolizumab for treating severe eosinophilic asthma

Technology appraisal guidance
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www.nice.org.uk/guidance/ta671

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

This guidance replaces TA431.

1 Recommendations

1.1 Mepolizumab, as an add-on therapy, is recommended as an option for treating severe refractory eosinophilic asthma, only if:

- it is used for adults who have agreed to and followed the optimised standard treatment plan and
- the blood eosinophil count has been recorded as 300 cells per microlitre or more and the person has had at least 4 exacerbations needing systemic corticosteroids in the previous 12 months, or has had continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months or
- the blood eosinophil count has been recorded as 400 cells per microlitre or more and the person has had at least 3 exacerbations needing systemic corticosteroids in the previous 12 months (so they are also eligible for either benralizumab or reslizumab).

  Mepolizumab is recommended only if the company provides it according to the commercial arrangement.

1.2 If mepolizumab, benralizumab or reslizumab are equally suitable, start treatment with the least expensive option (taking into account drug and administration costs).

1.3 At 12 months:

- stop mepolizumab if the asthma has not responded adequately or
- continue mepolizumab 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.

1.4 These recommendations are not intended to affect treatment with mepolizumab that was started in the NHS before this guidance was published. People 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.

Why the committee made these recommendations

For severe refractory eosinophilic asthma, standard therapy alone does not work well enough. So people usually also have benralizumab or mepolizumab if:

- their blood eosinophil count is 300 cells per microlitre or more and
- they have had at least 4 severe exacerbations needing systemic corticosteroids in the previous 12 months or continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months.

People can have benralizumab or reslizumab if their blood eosinophil count is 400 cells per microlitre or more and they have had at least 3 severe exacerbations in the previous 12 months.

There is no evidence directly comparing mepolizumab with benralizumab and reslizumab. But an indirect comparison suggests that it works as well as benralizumab and reslizumab for people with a blood eosinophil count of 400 cells per microlitre or more.

Mepolizumab is cost saving compared with benralizumab and reslizumab. So it is now also recommended for people with a blood eosinophil count of 400 cells per microlitre or more and at least 3 severe exacerbations in the previous 12 months.

2 Information about mepolizumab

Marketing authorisation indication

2.1 Mepolizumab (Nucala, GlaxoSmithKline) has a marketing authorisation in the UK as an 'add-on treatment for severe refractory eosinophilic asthma in adults, adolescents and children aged 6 years and older'.

Dosage in the marketing authorisation

2.2 Mepolizumab is available as a powder for solution for injection in vials, or as a solution for injection in pre-filled syringes and pre-filled pens. The dosage schedule is available in the summary of product characteristics.

Price

2.3 The list price of mepolizumab is £840 per 100 mg dose (excluding VAT; BNF online, accessed November 2020). The company has a commercial arrangement. This makes mepolizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by GlaxoSmithKline, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence. The company proposed that this technology be considered in a fast track appraisal using cost-comparison methodology.

New treatment option

People with severe eosinophilic asthma will welcome a new treatment option

3.1 Severe refractory eosinophilic asthma is a debilitating condition, which does not respond well enough to standard therapy and has many distressing symptoms. Asthma exacerbations can happen without warning, be life threatening, cause fear, and result in hospitalisation and intubation. People with uncontrolled severe eosinophilic asthma are often unable to work and may need help with day-to-day activities because of the symptoms. These physical and psychological pressures negatively affect quality of life. The patient experts highlighted an urgent need for more biological treatments for people who are not eligible for benralizumab or reslizumab or whose asthma does not respond to them. These people would otherwise need more intensive treatment with oral corticosteroids, which are associated with major side effects including diabetes, glaucoma, weight gain, loss of bone density and raised blood pressure. The clinical experts explained that the clinical community would welcome treatment criteria for biologicals to be standardised. The committee concluded that people with severe eosinophilic asthma with a blood eosinophil count of 400 cells per microlitre or more and at least 3 severe asthma exacerbations would welcome a new treatment option.

Clinical effectiveness

The indirect treatment comparison of mepolizumab, benralizumab and reslizumab is appropriate

3.2 NICE originally recommended mepolizumab for treating severe refractory eosinophilic asthma in adults with:

- a blood eosinophil count of 300 cells per microlitre or more and
- at least 4 severe exacerbations needing systemic corticosteroids in the past 12 months or if they have had continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months.

The company proposed extending this recommendation, in line with NICE's technology appraisal guidance on benralizumab and reslizumab, to include people with:

- a blood eosinophil count of 400 cells per microlitre or more and
- at least 3 severe exacerbations needing systemic corticosteroids in the past 12 months.

The company's evidence submission did not include any head-to-head trials directly comparing mepolizumab with benralizumab and reslizumab. It presented an indirect treatment comparison (ITC) of mepolizumab, benralizumab and reslizumab in severe eosinophilic asthma. The ITC included 9 placebo-controlled studies. The primary outcomes included:

- exacerbation needing treatment with oral corticosteroids
- exacerbation needing an emergency department visit or hospitalisation

- Asthma Control Questionnaire score and change from baseline pre-bronchodilator forced expiratory volume in 1 second.

  The committee noted the limitations of the company's ITC, namely that potentially relevant studies were omitted. The 75 mg treatment arms from DREAM and MENSA were omitted to ensure that the data reflected the licensed dose of 100 mg. The ERG was unable to fully assess the effect of excluding these on the final efficacy results. It considered that omitting ZONDA and SIRIUS from the ITC was appropriate because of their different primary outcomes. The ERG also noted variation between studies in length of follow up, dosing and administration, asthma severity, blood eosinophil counts and previous exacerbations. But it recognised that most of the pairwise meta-analyses had low heterogeneity. It also noted that corticosteroid reduction was among the outcomes missing from the ITC. However, its clinical advisers suggested that a reduction in exacerbations may also imply a reduction in corticosteroid use so the ERG did not consider this to be an issue. The committee concluded that the ITC of mepolizumab, benralizumab and reslizumab is appropriate.

There is sufficient evidence that mepolizumab has comparable efficacy to benralizumab and reslizumab

3.3 The results of the ITC for the primary outcomes broadly favoured mepolizumab over benralizumab and reslizumab for the subgroups in the trials with an eosinophil count of 400 cells per microlitre or more. But no evidence of a difference between treatments was found when the full trial populations were compared. The analysis for the comparison of mepolizumab with benralizumab and reslizumab was done for people with:

- a blood eosinophil count of 400 cells per microlitre or more and

- at least 1 severe exacerbation in the reslizumab arm or 2 severe exacerbations in the mepolizumab and benralizumab arms.

  However, the ERG stated that although this broader subgroup was not exactly aligned to the population being considered, it was closer than any other analysis. The ERG confirmed that there was a low risk that mepolizumab was less effective than benralizumab and reslizumab for severe eosinophilic asthma. The committee concluded that there was sufficient evidence that mepolizumab has comparable efficacy to benralizumab and reslizumab.

Cost comparison

A 10-year time horizon is more appropriate for decision making

3.4 The company did a cost comparison of mepolizumab with benralizumab and reslizumab. The costs were presented over a 1-year time horizon and were not discounted. The analysis compared:

- mepolizumab 100 mg; a powdered vial for mixing, a pre-filled syringe and pre-filled pen, administered subcutaneously every 4 weeks
- benralizumab 30 mg; a pre-filled syringe and pre-filled pen, administered subcutaneously every 4 weeks for the first 3 doses, then every 8 weeks and

- reslizumab with a weight-dependent dose (assuming a mean weight of 78 kg for the UK adult population); concentrate for intravenous infusion administered every 4 weeks.

  The analysis included drug, administration and monitoring costs. Oral corticosteroid costs were not included in the analysis. The analysis assumed that there were no differences in adverse event costs based on a Cochrane review that found no excess serious adverse events with any anti-interleukin-5 treatments (such as mepolizumab, benralizumab and reslizumab). It was uncertain whether a 1-year time horizon was sufficient to capture the key differences in costs between treatments. This was particularly because of the loading dose for benralizumab, and differences in dosing frequency and administration costs over time. However, an ERG scenario showed that mepolizumab remained cost saving over a 10-year time horizon. The ERG did not consider monitoring costs to be a key driver of the results. The committee concluded that a 10-year time horizon was more appropriate for decision making.

Self-administration has a small effect on the cost-comparison results

3.5 The committee questioned the proportion of people likely to self-administer the drug and the effect of this on savings with mepolizumab. The company explained that around 97% of people are currently self-administering and only 3% need mepolizumab to be given by a nurse. The clinical experts advised that the largest saving from those self-administering is in secondary care, with savings related to pharmacy and nurse time. However, people being set up for self-administration would need slightly longer appointments. The ERG explained that in the context of the drug costs, administration cost differences have little effect. The committee concluded that self-administration has a small effect on the cost-comparison results and the incremental savings with mepolizumab are mainly related to lower drug costs.

Mepolizumab results in cost savings when compared with benralizumab and reslizumab

3.6 The company's cost comparison included a range of assumptions for:

- administration and monitoring costs
- oral corticosteroid use
- the comparable safety profile of mepolizumab, benralizumab and reslizumab over a 1-year time horizon.

Assuming equivalent effectiveness and based on the list price for all treatments, mepolizumab had incremental cost savings compared with benralizumab and reslizumab. Mepolizumab remained cost saving in the additional ERG scenario over a 10-year time horizon. The committee concluded that, at list price, mepolizumab was cost saving compared with benralizumab and reslizumab for people with an eosinophil count of 400 cells per microlitre or more, and at least 3 severe exacerbations per year. Mepolizumab, benralizumab and reslizumab are available to the NHS with confidential commercial arrangements. The ERG analysis including these commercial arrangements did not change the committee's conclusion.

Mepolizumab is recommended

3.7 The committee concluded that mepolizumab met the criteria to be recommended based on a cost comparison, because the overall health benefits are similar to those of benralizumab and reslizumab. The committee concluded that mepolizumab could be recommended as an option for treating severe refractory eosinophilic asthma in adults with:

- a blood eosinophil count of 300 cells per microlitre or more and at least 4 exacerbations needing systemic corticosteroids in the previous 12 months or continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months or
- a blood eosinophil count of 400 cells per microlitre or more and at least 3 exacerbations needing systemic corticosteroids in the previous 12 months.

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. Because mepolizumab has been recommended through the fast track appraisal process, NHS England and commissioning groups have agreed to provide funding to implement this guidance 30 days after 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 person has severe eosinophilic asthma and the doctor responsible for their care thinks that mepolizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

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