Review proposal of TA431; Mepolizumab for treating severe eosinophilic asthma

TA431 was published in January 2017 and scheduled to be considered for review in 2020. An early review has been requested by the company that markets mepolizumab (GSK).

1. Decision

A review of the appraisal will be planned into the NICE's work programme. This review will be conducted as a single technology appraisal.

2. Rationale

The company that markets mepolizumab (GSK) has requested that NICE align the mepolizumab recommendation to that for benralizumab in TA565.

Mepolizumab was the first biological treatment targeting interleukin-5 to be appraised for the treatment of severe refractory eosinophilic asthma. Reslizumab was the second and was recommended in a different population to mepolizumab, reflecting different inclusion criteria in the clinical trial evidence (TA479). Benralizumab, a biological agent that targets the human interleukin-5 receptor, was the third agent to be appraised for the indication and was recommended both for people eligible for mepolizumab and for people eligible for reslizumab.

In the appraisal of benralizumab (TA565), the company (AstraZeneca) did not do a conventional network meta-analysis to compare benralizumab with reslizumab and mepolizumab, because of the significant differences in the patient populations in the trials for these drugs. The company argued that it is more appropriate to adjust for differences in patient characteristics between the trials using an anchored matched-adjusted indirect comparison (MAIC). However, this was only considered feasible for the comparison with mepolizumab. For the comparison with reslizumab the company made the simple assumption that benralizumab and reslizumab had the same efficacy.

In TA565 the committee concluded that benralizumab and mepolizumab were essentially similar in terms of their clinical and cost effectiveness. Once the updated patient access scheme (PAS) price for benralizumab and the PAS price for mepolizumab are used in the model, the ICER is below £20,000 per QALY gained in the people who would be eligible for treatment with mepolizumab according to TA431. However, this ICER was based the MAIC, which found superior benefit for benralizumab, which the committee did not accept as robust. The committee was reassured by a cost-comparison done by the ERG which found the 2 drugs have similar long-term costs and therefore concluded that benralizumab could be recommended for the mepolizumab-eligible population. For the comparison with reslizumab, although the simple assumption of clinical equivalence was questionable, the committee concluded that it was reasonable to assume that they are not very different. When the PAS prices for benralizumab and reslizumab were used in the ERG analysis, benralizumab was clearly cost effective compared with reslizumab. Therefore, the committee concluded that benralizumab could be recommended for the reslizumab-eligible population.

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This means that there is a population for whom benralizumab is recommended, but mepolizumab is not: that is, people with an eosinophil count of 400 cells per microlitre or more and who have had exactly 3 exacerbations in the last year and are not on oral corticosteroids. In this context GSK argue that the recommendations for mepolizumab and benralizumab should be aligned.

In support of this request, GSK has supplied a published indirect comparison (Busse et al., 2019). This review concluded that there was a statistically significant reduction in clinically significant exacerbations with mepolizumab compared with benralizumab in all subgroups according to baseline blood eosinophil count and compared with reslizumab in the subgroup with a baseline blood eosinophil count of 400 cells/microlitre or greater (reflecting the clinical trial population for reslizumab). When the 'unadjusted' population, which did not take baseline blood eosinophil counts into account, was considered, no statistically significant differences in clinically significant exacerbations were seen between the 3 treatments.

Given that the committee has already concluded that benralizumab and mepolizumab have similar clinical effectiveness, a cost comparison, fast track appraisal may be appropriate should the company wish to continue down this route.

3. Summary of new evidence and implications for review

Has there been any change to the price of the technology(ies) since the guidance was published?

There is a patient access scheme in place for mepolizumab. GSK will continue this without any changes.

Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?

Since the publication of TA431, the licence for mepolizumab has been extended to paediatrics aged 6 years or more. As NHS England routinely apply the funding direction for products appraised in adults to paediatric licence-extensions where appropriate, this change alone would not prompt a review.

In addition, there are licences for two other formulations, a pre-filled syringe and a pre-filled pen. These formulations allow self-administration of the mepolizumab by the patient if their healthcare professional determines that it is appropriate. Note that the 100 mg solution for injection in pre-filled pen and pre-filled syringe are only indicated in patients 12 years and above. The option for self-administration has also been added to the marketing authorisation for similar formulations of the comparator product, benralizumab.

Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?

No, the main issue is the availability of competitor products.

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Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?

An update of NG80 is planned, but it is not anticipated that this will include a review of treatments for eosinophilic asthma.

4. Equality issues

No issues were identified during the scoping or the appraisals.

Decision paper sign off

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Appendix A – Information from existing guidance

1. Original remit

To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for treating severe eosinophilic asthma

2. Current guidance

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

- the blood eosinophil count is 300 cells/microlitre or more in the previous 12 months and
- the person has agreed to and followed the optimised standard treatment plan and
    - has had 4 or more asthma 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 and
- the company provides the drug with the discount agreed in the patient access scheme.

1.2 At 12 months of treatment:

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

An adequate response is defined as:

- at least 50% fewer asthma exacerbations needing systemic corticosteroids in those people with 4 or more exacerbations in the previous 12 months or
- a clinically significant reduction in continuous oral corticosteroid use while maintaining or improving asthma control.

1.3 This guidance is not intended to affect the position of patients whose treatment with mepolizumab was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

3. Research recommendations from original guidance

Not applicable.

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Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the STA/FTA process.	A review of the appraisal will be planned into the NICE's work programme. This will be conducted as a cost-comparison FTA.	**Yes**
The decision to review the guidance should be deferred to a specific date or trial.	NICE will reconsider whether a review is necessary at the specified date.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

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Options	Consequence	Selected – 'Yes/No'
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider.	No
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

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Appendix C – Other relevant information

Relevant Institute work

Published

Asthma (2019) NICE pathway

Asthma (2013) NICE quality standard 25

Asthma: diagnosis, monitoring and chronic asthma management (2017) NICE guideline 80

Benralizumab for treating severe eosinophilic asthma (2019) NICE technology appraisal guidance 565

Reslizumab for treating severe eosinophilic asthma (2017) NICE technology appraisal guidance 479

In progress

Asthma: diagnosis, monitoring and chronic asthma management (partial update of NG80) Expected publication date: 29 January 2020

Details of changes to the marketing authorisation for the technology

Marketing authorisation and price considered in original appraisal

Indication: 'add-on treatment for severe refractory eosinophilic asthma in adult patients'.

List price: £840 per dose (excluding VAT)

PAS price: £[redacted] per dose (excluding VAT)

Proposed marketing authorisation (for this appraisal) and current price

Current indication: ‘add-on treatment for severe refractory eosinophilic asthma in adults, adolescents and children aged 6 years and older'.

The list price and PAS price remain unchanged.

References

Busse W, Chupp G, Nagase H, et al. (2019). Anti-IL-5 treatments in patients with severe asthma by blood eosinophil thresholds: Indirect treatment comparison. The Journal of allergy and clinical immunology 143:190-200

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