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Reslizumab for treating asthma with elevated blood eosinophils inadequately controlled by inhaled corticosteroids: ERG critique of the company's updated analyses

Confidential appendix to Evidence Review Group report

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This appendix contains commercial in confidence information which is highlighted in blue and underlined

1. Introduction

The second NICE Appraisal Committee Meeting (ACM) for the resilizumab Single Technology Appraisal was held on 11th April. In response to the evidence discussed at the ACM, the NICE Appraisal Committee issued a 2nd Appraisal Consultation Document (ACD). The company (Teva Pharmaceuticals) has provided their response to the 2nd ACD.

In this report we provide an independent critique of the additional analyses submitted by the company.

The company's revised base case is shown in Table 1. This has the following differences from the previous company base case:

- no adjustment of exacerbation rates for the best supportive care arm, so as to reflect the rates observed in clinical practice in the UK;
- changes to the utility values for severe exacerbations;
- vial-based dosing including both 100-mg and 25-mg vials; and
- a new Patient Access Scheme (PAS) with a simple discount for the cost of resilizumab of [redacted].

The changes made by the company are discussed further in the following sections.

Table 1 Revised company base case for adults with severe eosinophilic asthma and 3 exacerbations in the previous year

	Total costs			Total QALYs			ICER
Scenario	**Reslizumab**	**BSC**	**Incremental**	**Reslizumab**	**BSC**	**Incremental**	
ACD1 Base case	[redacted]	£83,417	[redacted]	15.08	11.99	3.09	£25,408
Revised base case	[redacted]	£61,713	[redacted]	15.84	13.64	2.20	£29,870

2. ERG's checks and critique of the company's analyses

The ERG has checked the results produced by the company by running the company's economic model and is able to replicate the results the results shown in Table 1 by making the changes described by the company.

2.1 Exacerbation rate

The company's revised base case uses transition probabilities for resilizumab and best supportive care estimated based on patients who had experienced 3 or more exacerbations in the year previous year. Their analysis makes no adjustment to the exacerbation rates for best supportive care, so as to reflect 'real world' exacerbation rates observed in clinical practice in the UK.

The changes made by the company for exacerbation rates for best supportive care are consistent with NICE committee's preferred approach for the exacerbation rate for best supportive care.

2.2 Utility values for severe exacerbations

The company provided data from studies 3082 and 3083 on the duration of severe exacerbations in patients who had severe eosinophilic asthma and 3 or more exacerbations in the previous year. The mean length of a severe exacerbation for patients receiving resilizumab was [redacted] days, compared to [redacted] days for patients on placebo. A severe exacerbation was defined as an exacerbation 'requiring the use of (additional) systemic steroids'.

The ERG notes the following potential limitations to these exacerbation duration data:

- These data are subject to the same limitations as other outcomes from studies 3082 and 3083, i.e. they may not be reflective of the responses of patients who have lower eosinophil counts and a need for oral corticosteroids (section 4.4 in the 2nd ACD).
- The statistical comparison of severe exacerbation durations was post-hoc (i.e. testing a hypothesis suggested by the data), which may result in false positives; however, this does not influence the company's calculation of utilities.
- The data on severe exacerbation durations are new (not available in the company's submission or clinical study reports), so the ERG could not check them.
- The ERG was unable to find any comparable data on severe exacerbation durations experienced in clinical practice against which to compare the company's data. The effect of reslizumab in reducing the duration of severe exacerbations is clinically plausible, but there is uncertainty as to how closely the company's data would match 'real world' severe exacerbation durations and the variability associated with them.

In the company's original analysis a single utility value was used for both resilizumab and best supportive care and this was applied to the duration of the full model cycle (4 weeks).

The company's new analysis provides specific utility values for each comparator and these have been weighted according the duration of the severe exacerbations (as given above), to account for the fact that severe exacerbations do not last for the full model cycle. The overall mean utility for severe exacerbation in each model cycle is calculated from the weighted utility for the time with severe exacerbation plus the weighted utility for the exacerbation-free ('uncontrolled' utility) remainder time of the model cycle. The ERG considers the calculation used to derive the new utility values for severe exacerbation to be appropriate.

The recalculated severe exacerbation values were 0.54 for patients receiving resilizumab and 0.50 for patients receiving best supportive care, compared to the previously used utility value for severe exacerbation of 0.51 for all patients.

As stated in the ERG report, the utility value estimates for severe exacerbations are somewhat uncertain due to the lack of robust health-related quality of life data. However, the ERG considers the changes the company has made regarding utility values for severe exacerbation in the company's response to the 2nd ACD are reasonable, given the limited availability of evidence. The ERG notes that changing the utility values in this way reduces the ICER by about £1000.

2.3 Dosing

The NICE committee concluded in the 2nd ACD that 'the 25-mg vial could be considered and that any positive recommendation would only be made based on the availability of this size of vial'. The company therefore proposed that vial-based dosing is appropriate, using a combination of 25-mg and 100-mg vials according to dosing based on patients' weight, to minimise wastage. This differs from the previous company analyses that used only 25-mg vials or only 100-mg vials. The ERG considers that if 25-mg vials are made available (and are acceptable to clinicians), then use of these in vial-based dosing would be reasonable.

2.4 Revised Patient Access Scheme

The company has submitted a revised PAS which reduces the acquisition costs of resilizumab from the previous PAS discount of [redacted] to the revised PAS of [redacted]. The revised PAS price for a 25-mg vial of resilizumab is [redacted] compared to the list price of [redacted].

2.5 Effects of individual amendments

The company has provided a breakdown of the effect of each of the amendments on the ICER and is shown in Table 2 (reproduced from company's ACD response Table 1).

Table 2 Summary of ICERs with each implemented amendment

Scenario	ICER
Base case submitted in response to ACD1	**£25,408**
• No adjustment on exacerbation rate	£43,064
• Revised utilities for severe exacerbation, no adjustment on exacerbation rate	£42,025
• Vial-based dosing, no adjustment on exacerbation rate	[redacted]
• Revised PAS, no adjustment on exacerbation rate	[redacted]
Revised base case with all amendments	**£29,870**

3. Summary

The ERG has reviewed the updated analyses made by the company in response to the 2nd ACD. We have checked the analyses and replicated the results. We consider that the company's amendments and their results presented are reasonable, given the limitations of the available data.