Asthma UK response to NICE's second appraisal consultation document on mepolizumab for treating severe refractory eosinophilic asthma

1. Has all of the relevant evidence been taken into account?

Asthma UK considers mepolizumab to be a novel and innovative treatment that seeks to address an unmet need for people with severe eosinophilic asthma. While we appreciate that NICE has accepted some of the points we submitted in response to the first appraisal consultation document (ACD) around the target population for mepolizumab, some key considerations remain unaddressed and therefore many of the areas of concern are unchanged from our previous submissions – in particular around oral corticosteroid (OCS) use.

The Committee heard from one patient expert on the serious reality of living with severe asthma. Another we have worked with describes their experience of the condition in clear terms:

"On a bad day I feel like I'm drowning and I can't reach the surface of the water and I'm going to burst, yet a tiny, tiny bit of air keeps me alive. It's very scary – I feel like I'm living with a time bomb and if I have a bad attack I say to myself 'Is this the one that will kill me?'"

People with severe asthma almost always find themselves taking very high doses of medicines for a long time and the side effects of these medicines, especially long-term OCS, are often very serious. We were disappointed that a study by Sweeney et al. did not appear to be considered in relation to comorbidities resulting from severe asthma requiring systemic corticosteroid therapy (http://dx.doi.org/10.1136/thoraxjnl-2015-207630). This is a recent study, published online earlier this year, which presents data from two large severe asthma populations (the Optimum Patient Care Research Database and the British Thoracic Difficult Asthma Registry) and shows that OCS use results in a higher prevalence of comorbidities - including type II diabetes, hypertension and osteoporosis.

The committee has again recognised that some benefits related to avoiding the significant adverse effects of OCS use had not been fully captured in the QALY measure (4.28). There is a significant gap in high quality data that considers the morbidity due to OCS use in people with severe asthma, but this should not mean that NICE cannot consider the evidence that is available. The Sweeney et al. paper has been described as "the best estimate yet of the burden of OCS treatment in severe asthma" (Choo & Pavord 2016, http://thorax.bmj.com/content/71/4/302.full). We were therefore disappointed that this was not included in the assessment of mepolizumab – this should be reconsidered by the committee and factored into the incremental cost-effectiveness ratio (ICER), in addition to quality-of-life benefits to carers. We note that this point was also made by both the manufacturer and British Thoracic Society in their responses to the ACD.

Estimating the impact of the effects of OCS use is a crucial area that needs to be addressed, particularly given that from a patient perspective, reduced use is a key benefit of any future treatment. Mepolizumab is the first in what we anticipate will be a next generation of treatments for people with severe eosinophilic asthma. Unless the true

impact of OCS use is captured, we are concerned that similar novel and innovative treatments for severe asthma will not be comprehensively assessed.

One patient wrote to Asthma UK recently to give us an insight on how mepolizumab had improved their day-to-day life. His asthma meant that he would be totally out of breath after a short walk, light-headed, and gasping for breath. After taking part in one of the trials for mepolizumab in Southampton he was able to act as a sole carer to his wife over several years before her death – in his words, he "could not have done this without the aid of the drug." Every effort should be made to ensure this is made available to patients. Whilst this is only one example Asthma UK believes this brings to the fore the lived experience of severe asthma and the impact that it has on people's quality of life and the role that they are able to play in society through work and family life. Innovative new treatments that enable people to play a greater role, live more independently and enable people to do more through employment and in family life are urgently needed for this cohort.

2. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

We note that the committee has remained unchanged on the issue of how to capture the health-related quality-of-life benefits of mepolizumab in its model. Clinicians we consulted as part of our response to the first ACD agreed that the St George's Respiratory Questionnaire (SGRQ) was a more appropriate method than EQ-5D for measuring improvements in quality of life for people with severe asthma due to it being able to effectively capture exacerbations.

As highlighted by the manufacturer, in the DREAM study, a third of patients reported "perfect health" on the EQ-5D at baseline. Severe asthma is a condition where between attacks patients can be considered well in between exacerbations of their condition. However, quality of life is severely impaired during attacks and, in many patients with severe eosinophilic asthma, by the treatment required to treat and prevent these attacks.

EQ-5D is effective in capturing some measures of patients' health-related quality of life, but often these are not key issues for people with severe asthma. In contrast, SGRQ focuses more on capturing the quality of life measures of primary concern to people with a severe respiratory condition - measuring symptom-control (such as cough, wheeze, breathlessness, frequency of attacks), activity (focusing on limitations due to breathlessness), and impact (which includes a range of factors including side effects of prescribed medication). Similarly we would not expect these factors of concern to people with severe asthma to be applicable to a number of non-respiratory conditions. NICE has to appreciate that in relying on EQ-5D measures it is missing the true impact this treatment has on severe asthma.

We do not believe that "perfect health", as captured in EQ-5D, is a true starting point for people with severe asthma, as they have to find a way to cope with persistent symptoms that can lead to lack of sleep, social isolation, feelings of despair and depression, low activity levels, weight gain and increased dependence on family and carers – their baseline for what constitutes good health will naturally be set at a lower level for a condition they have had to manage throughout their lives. If the EQ-5D model is unable to capture

improvements in quality of life in a third of the population modelled, this highlights the need for a more appropriate model. We urge NICE to reconsider using data from SGRQ in its model to help to fully capture the benefits from this treatment, which we believe are significant. For example, the MENSA study of mepolizumab showed that the baseline scores on the SGRQ in those with severe eosinophilic asthma were equivalent to those seen in patients with severe COPD (Ortega et al. 2014, http://www.nejm.org/doi/full/10.1056/NEJMoa1403290). Treatment with mepolizumab was associated with a 10 point improvement in SGRQ in the population accepted as being potentially eligible for treatment based on the latest ACD. The improvement in this measure is roughly 3 times more than has been found for Seretide vs placebo in severe COPD (Calverley et al. 2007, http://www.nejm.org/doi/full/10.1056/NEJMoa063070).

We appreciate that the committee has considered two separate models on which to model age-related mortality. While Roberts et al. may look at a larger population and a broader range through its age stratification, it is likely to underestimate the number of deaths due to it not including comorbidities. In contrast, Watson et al. includes deaths from all causes after hospitalisation for asthma, so including this in the ICER model is more likely to capture mortality from comorbidities and give a more accurate picture of asthma mortality.

3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

Asthma UK remains deeply disappointed in the draft recommendation, and is extremely concerned that the ICER still fails to take key considerations into account relating to asthma. Mepolizumab is an innovative treatment which meets an unmet need for severe eosinophilic asthma and has shown significant clinical benefit in clinical trials. We strongly urge the appraisal committee to reconsider this draft decision.

NICE must find a way to take into account the impact on improving the lives of carers, and the health and quality of life benefits of reducing OCS, which as highlighted by the appraisal committee would reduce the ICER.

4. 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?

As mentioned previously, there is a substantial unmet need for people with severe asthma in the treatment options available to them. People with severe asthma have very limited treatment options that involve high doses of drugs with toxic and damaging side effect profiles and significant long-term health impacts. Mepolizumab could provide an effective treatment option for people with severe eosinophilic asthma who currently have no treatment option. The rejection by the appraisal committee of this innovative treatment will mean people with severe eosinophilic asthma remain disadvantaged through a lack of access to effective treatments for their condition.

Additional comments on the ACD

None