CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

Mepolizumab (Nucala®, GlaxoSmithKline plc.) for the Treatment of Severe Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks

Summary of Public Comments Received on Initial Draft Report and ICER Response

The Institute for Clinical and Economic Review (ICER) values the opportunity to receive and respond to public comment on its work products by interested stakeholders. There were five sets of stakeholder comments submitted in response to the initial draft CTAF report on mepolizumab (Nucala®, GlaxoSmithKline plc.) for the treatment of severe asthma with eosinophilia that was posted on December 21, 2015. Below is a summary of the major comments received, organized by major report component, as well as responses from the ICER team and its research collaborators, including any major changes made to the report.

Evidence Review

- The focus of attention in our review was on studies that featured the FDA-approved 100 mg subcutaneous dose formulation of mepolizumab. The initial draft report included data from the DREAM study[1] of a 75 mg intravenous formulation of mepolizumab in our review of potential harms; stakeholder comments suggested that we also consider effectiveness data, as pharmacodynamics studies indicate that the two formulations are comparable in their systemic activity.[2] We have revised the report to include additional data from DREAM in our review of effectiveness.

- Stakeholders also stated that evidence of durability of effect was tested in two open-label extension studies that enrolled patients from previous mepolizumab trials. Although one of these studies is now complete, we are not aware of any data from this study that have been published or presented in a public forum. We have added descriptions of both studies to Appendix E (Ongoing Studies) of the revised draft report.

- Other comments suggested that we underestimated the long-term benefits of mepolizumab because use of the drug is likely to attenuate airway remodeling in at least some patients with severe asthma. While this may prove to be true, we have identified no evidence on this phenomenon—indeed, the open-label extension studies are intended to measure outcomes during long-term treatment, not observation after treatment has been stopped. No changes have been made to the revised draft report.

- The above comments were all used in support of arguments that we should raise our level of certainty beyond moderate certainty of a comparable or better net health benefit. In our view, the additional data described in these comments were not compelling enough to change our level of certainty.

- Other stakeholders highlighted the marked decreases in asthma exacerbations in the placebo arm of available trials noted in our review, suggesting that this warranted further discussion of the need for patient and provider educations, revising payment policies to optimize access to standard treatment, and removal of barriers to patient access. We plan to make this an important component of our roundtable discussion at the upcoming CTAF public meeting on February 12.

Comparative Value

- Stakeholders criticized our decision not to model omalizumab as an explicit comparator in our cost-effectiveness analysis. We stand by the rationale for our decision: that such an analysis was not appropriate because there are no available head-to-head data, indirect comparisons, or even single-arm evidence in the subpopulation of patients with severe, persistent, IgE-mediated eosinophilic asthma who would be naïve to either therapy. We have revised our report, however, to reflect the increased price of omalizumab for the average patient, based on additional stakeholder comment.

- We also received comments that the common thresholds used for cost-effectiveness findings in the U.S. ($50,000-$150,000 per QALY) may not be appropriate when assessing primarily employed populations, such as adults suffering from severe asthma. We have revised the report to acknowledge this, but have also noted that the current estimate for mepolizumab cost-effectiveness exceeds even these thresholds.

- Other stakeholders commented that use of high-priced medications in patients already using multiple agents might increase the financial burden to patients through increased copayments or coinsurance. We have revised the report to note the limitation of our payer perspective—namely, that total costs borne by the payer are estimated without separate calculation of the proportion of costs borne by the patient—but also acknowledge that this proportion is highly dependent on individual payer and benefit design.

- Stakeholders requested clarity on how trial data were extrapolated to assume lifetime clinical effects in the modeling. We have added text clarifying that trial-based effects were assumed to persist over the model time horizon; we note, however, that model time horizons ranging from 1 to 50 years were tested in sensitivity analysis, with relatively little impact on our findings.

Other Comments

- Several stakeholders requested that we modify language describing mepolizumab in the voting questions and draft report to be consistent with FDA-approved prescribing information. Specifically, the indication is now described as “severe asthma with an eosinophilic phenotype,”

and requirements for reconstitution and administration by a healthcare professional are now included in the report.

References:

1. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicenter, double-blind, placebo-controlled trial. *Lancet* 2012;380:651-659.

2. Pouliquen IJ, Kornmann O, Barton SV, et al. Characterization of the relationship between dose and blood eosinophil response following subcutaneous administration of mepolizumab. Int J Clin Pharmacol Ther 2015;53:1015-1027.