For Treating Severe Eosinophilic Asthma

Does this new drug meet an important need?

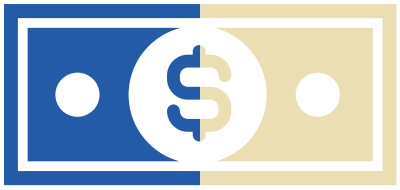
The Burden of Asthma

Number of people in the U.S. with asthma: 22 million

5–10% have severe asthma

Annual medical costs to treat asthma: $50 billion

50% of costs go to treat individuals with severe asthma



Source: CDC

The Therapeutic Role of Mepolizumab

Mepolizumab (Nucala®, GlaxoSmithKline) is a humanized monoclonal antibody against interleukin-5 (IL-5), the key promoter of eosinophil growth. Mepolizumab is an injectable drug that is administered every four weeks in a physician's office for the treatment of severe eosinophilic asthma in patients 12 and older. Eosinophils play a significant role in the inflammation related to asthma. Many patients with severe asthma have frequent exacerbations, emergency department (ED) visits, and chronic oral corticosteroid (OCS) use. Mepolizumab is given in addition to standard care. Chronic OCS use is associated with infections, diabetes, myopathy, obesity, glaucoma, depression, delirium, hypertension, adrenal suppression, cataracts, and more.

Annual Cost of Mepolizumab

Standard Care*
$5,738

Mepolizumab**
$32,500

* Includes Advair 500/50, one inhalation twice daily (2015 Redbook WAC is $407.51 per 30 days) and quarterly office visits (4 × $195)

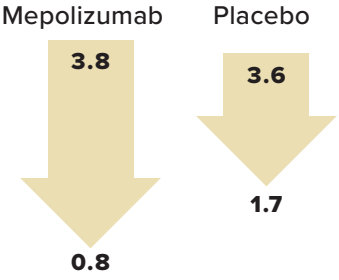
** 32,500 is the list price. The cost of standard care, which would be needed in addition to mepolizumab, is not included in this amount.

How strong is the evidence that mepolizumab works?

Mepolizumab + Standard Treatment for Severe Asthma vs. Standard Treatment Alone

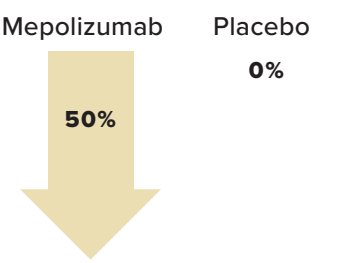
Absolute reduction in the number of significant exacerbations per year:*

* In the MENSA trial



Median percent reduction in oral corticosteroid dose:**

** In the MENSA trial



Patient quality of life:

- Average Asthma Control Questionnaire (ACQ) scores improved by 0.44 in the MENSA trial and by 0.52 in the SIRIUS trial compared to placebo (an improvement of 0.5 points is considered clinically significant)
- Average St. George's Respiratory Questionnaire (SGRQ) scores improved by 7 points in the MENSA trial, and by 5.8 points in the SIRIUS trial compared to placebo (an improvement of 4 points is considered clinically significant).

Sources of Uncertainty

- The long-term durability of the benefits of the therapy and the potential harms from modulation of the immune system are uncertain given the relatively small number of patients and the short duration of follow-up of studies in the peer-reviewed literature (6–8 months).
- There were very few adverse events in clinical trials. The greatest concern is that relatively uncommon side effects, such as opportunistic infections or anaphylaxis, will emerge as a larger group of patients is treated over several years.
- There were not enough patients studied who are of African descent or who are younger than 18 to draw any meaningful conclusions about the net health benefits of mepolizumab in these two important subgroups.

Given its cost, what is the drug's value to patients and the health care system?

Long-Term Cost-Effectiveness

$386,000 per QALY

Computer modeling of long-term clinical benefits and costs showed that quality of life for patients was improved. Overall costs, even considering some reduction in emergency room and hospital costs with treatment, were increased.

The incremental cost-effectiveness ratio, measured by calculating the cost per additional quality-adjusted life year (QALY), was approximately $386,000. The cost per QALY range that represents "reasonable" value in the US is $50,000-$150,000 so **mepolizumab does not represent good value for money in the long-term.**

Potential Short-Term Budget Impact

$596 million per year

Approximately 320,000 individuals in the US would be eligible for treatment with mepolizumab. If insurers were not to apply strict coverage criteria, we estimate that approximately 10% of all eligible patients would be prescribed the drug over the first five years after FDA approval. Under these assumptions the total potential budget impact over five years would be $3 billion, with an average annual budget impact of $596 million. This figure does not exceed ICER's annual threshold of $904 million for the potential budget impact at which a drug would overly strain affordability of the health care system so **mepolizumab does not pose a substantial threat to health system affordability in the short term.**

ICER's Value-Based Price Benchmark

$7,787 to $12,116

- This price range represents a 63%-76% discount from the list price of $32,500.
- No additional price reduction would be necessary to avoid a substantial threat to health system affordability

ICER's value-based price benchmark is comprised of two components: a range associated with the prices needed to achieve long-term cost-effectiveness between $100,000-$150,000 per QALY; and, if necessary, a lower price at which short-term potential budget impact does not threaten overall health system affordability.

Public Deliberation and Evidence Votes

California Technology Assessment Forum (CTAF) Panel Votes

The California Technology Assessment Forum (CTAF) deliberated on key questions raised by ICER's report on mepolizumab at a public meeting on February 12, 2016. The results of the vote are presented below.

CTAF Panel Votes

1. For patients with severe asthma and with an eosinophilic phenotype, is the evidence adequate to demonstrate that the net health benefit of adding mepolizumab to standard of care is greater than that of standard of care alone?

CTAF Panel Vote:	**16 Yes (100%)**	**0 No (0%)**

2. Given the available evidence for patients with severe asthma and with an eosinophilic phenotype, what is the care value* of adding mepolizumab to standard of care vs. standard of care alone?

CTAF Panel Vote:	**8 Low (50%)**	**8 Intermediate (50%)**	**0 High (0%)**

3. Given the available evidence for patients with severe asthma and with an eosinophilic phenotype, what is the provisional health system value** of adding mepolizumab to standard of care vs. standard of care alone?

CTAF Panel Vote:	**12 Low (75%)**	**4 Intermediate (25%)**	**0 High (0%)**

* **Care value** represents a synthesis of four elements: comparative clinical effectiveness, incremental costs per outcomes achieved, other benefits or disadvantages, and contextual considerations. Care value represents the long-term perspective, at the individual patient level, on patient benefits and the incremental costs to achieve those benefits.

** **Provisional health system value** represents a judgment integrating consideration of the long-term care value of a new intervention with an analysis of its potential short-term budget impact if utilization is unmanaged.

Key Policy Implications and Recommendations

Payers

- Payers should implement reasonable prior authorization criteria for mepolizumab to ensure that the drug is prescribed to appropriate patients given the potential budget impact of adopting the drug and the CTAF Panel's vote that the drug holds low provisional health system value.

Providers

- Clinicians should ensure that patients most likely to benefit from mepolizumab therapy receive the drug; these patients are likely to have more severe asthma demonstrated by eosinophil counts closer to, or in excess of, 300 cells/μL and a history of severe exacerbations.
- Clinicians should be prepared to discuss the advantages and disadvantages of an office administered treatment with a monitoring requirement with patients.

Patients

- Patients should discuss the advantages and disadvantages of taking a drug that requires an office visit and observation period with their physician.
- Patients who are considering starting treatment with mepolizumab should ensure that they take their other controller medications as directed by their physician and avoid potentially hazardous overuse of rescue medications.

Manufacturers

- In bringing new drugs to market for an important unmet medical need, manufacturers should seek better alignment of pricing with estimates of long-term cost-effectiveness and should be sensitive to concerns surrounding short-term budget impact.
- Follow-up studies should be conducted to better understand long-terms effects of mepolizumab usage, and these studies should include a responder analysis so that clinicians are able to develop treatment cessation criteria.
- Manufacturers should conduct head-to-head studies of mepolizumab and omalizumab to demonstrate their relative effectiveness, especially within the population of patients eligible for both therapies.

Additional policy implications and recommendations can be found in the final report *Mepolizumab (Nucala®, GlaxoSmithKline plc.) for the Treatment of Severe Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks*.

Conclusion

In Summary

Adding mepolizumab to standard care for adult patients with severe eosinophilic asthma appears to confer clinical benefits in terms of reduced rates of exacerbation and improved quality of life.

However, at its current list price the ratio of the added costs to the added benefits of mepolizumab greatly exceed the range of $100,000-$150,000 per QALY that is used as a benchmark for reasonable long-term value.

Achieving levels of value more closely aligned with the amount of patient benefit would require price discounts of 63%-76% from the current list price of mepolizumab.

About ICER

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER's reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.

ICER's reports incorporate extensive input from all stakeholders and are the subject of public hearings through three core programs: the California Technology Assessment Forum (CTAF), the Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC) and the New England Comparative Effectiveness Public Advisory Council (New England CEPAC). These independent panels review ICER's reports at public meetings to deliberate on the evidence and develop recommendations for how patients, clinicians, insurers, and policymakers can improve the quality and value of health care. For more information about ICER, please visit ICER's website (www.icer-review.org).

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