



CALIFORNIA TECHNOLOGY ASSESSMENT FORUMSM

Mepolizumab (Nucala[®]) for Treatment of Severe Asthma with Eosinophilic Inflammation: Effectiveness, Value, and Value-Based Price Benchmarks

Final Background and Scope

November 18, 2015

Background:

The Centers for Disease Control and Prevention (CDC) estimates that 39.5 million Americans have been diagnosed with asthma at some time and that 22 million US residents currently have asthma.¹ Asthma causes the airways of the lungs to narrow or become blocked, making it hard to breathe. Many processes contribute to the narrowing, including tightening of the muscles around the airways, inflamed tissue lining the airways, and mucous plugging the airways. The disease follows a waxing and waning course with exacerbations initiated by allergens, cold weather, exercise, pollution, and other triggers. This leads to approximately 14.2 million office visits, 1.8 million emergency room visits, and 440,000 hospitalizations each year in the US.¹ The direct medical costs of asthma are estimated to be \$50 billion.¹ Individuals with severe asthma represent less than 5-10% of all individuals with asthma but account for approximately 50% of all costs. In addition to being treated with inhaled corticosteroids and long-acting beta agonist therapy, these patients are often treated with oral corticosteroids.² About half of individuals with severe asthma exhibit the eosinophilic phenotype with elevated eosinophil levels in both the blood and airways.³ Mepolizumab is a humanized monoclonal antibody to interleukin 5 (IL-5), a cell messenger that controls eosinophilic inflammation, and has been studied to determine if reduction in such inflammation leads to corresponding reductions in asthma exacerbation episodes and improved asthma control.

Report Aim:

This project will evaluate the health and economic outcomes of mepolizumab.

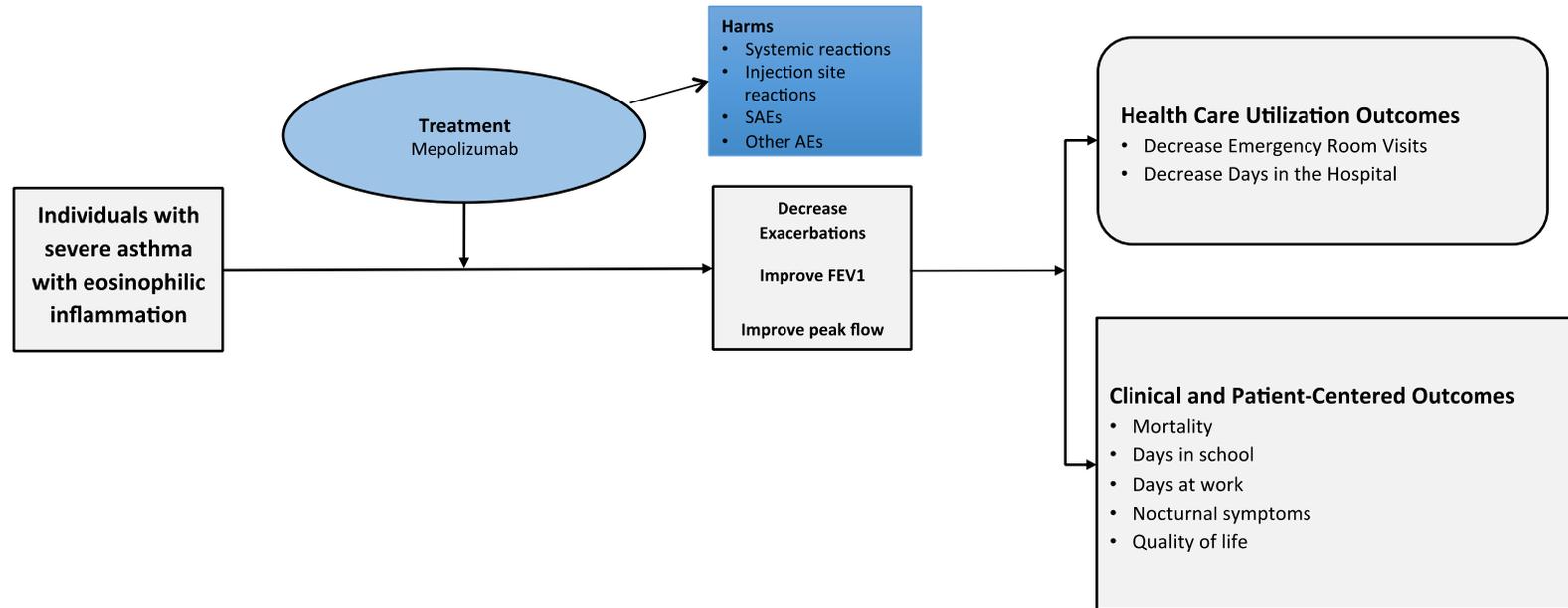
Scope of the Assessment:

The proposed scope for this assessment is described below using the PICOTS (Population, Intervention, Comparators, Outcomes, Timing, and Settings) framework. Evidence will be culled from Phase II or III randomized controlled trials and comparative cohort studies as well as high-quality systematic reviews where available. We will also include case series that meet certain quality criteria (e.g., sample retention, consecutive patients, clearly-defined entry criteria).

Analytic Framework:

The analytic framework for this assessment is depicted in Figure 1 on the following page.

Figure 1. Analytic Framework: Asthma Management with Mepolizumab



Note: SAEs: severe adverse effects; AEs: adverse effects; FEV₁: forced expiratory volume in 1 second

Populations

The population of focus for the review will be adults and children ages 12 years and older with severe, uncontrolled asthma and evidence of eosinophilic inflammation. Severe asthma is defined as asthma that requires either oral corticosteroids for >50% of the year or the combination of high dose inhaled corticosteroids and a long acting beta agonist or other controller medication (leukotriene inhibitor/theophylline) to maintain control.³ Uncontrolled asthma is defined by at least one of the following: frequent exacerbations (2+ bursts of oral steroid therapy lasting at least 4 days); serious exacerbations (hospitalization, ICU stay or mechanical ventilation); airflow limitation (FEV₁ <80% predicted); or poor symptom control (Asthma Control Questionnaire >1.5; Asthma Control Test < 20).³ Eosinophilic inflammation will be defined as a blood eosinophil level ≥150 cells/μL at initiation of therapy or ≥300 cells/μL in the prior 12 months. All individuals should be treated with high-dose inhaled corticosteroid therapy and at least one additional controller medication (e.g., long-acting beta agonists, leukotriene agonists, theophylline, oral corticosteroids).

Interventions

The intervention of interest will be mepolizumab 100 mg by subcutaneous injection once every 4 weeks, in conjunction with daily inhaled corticosteroid and other controller therapy.

Comparators

The comparators of interest will be placebo or oral corticosteroids added to daily inhaled corticosteroid and other controller therapy alone (control arms in the mepolizumab trials also received placebo injection). Omalizumab will be considered as a comparator for patients with severe eosinophilic asthma and elevated immunoglobulin E (IgE) levels.

Outcomes

This review will examine clinical and health care utilization outcomes related to asthma. Listed below are the outcomes of interest:

- Asthma control assessed by standard questionnaires (ACQ or ACT)
- Asthma exacerbations
- Asthma-related hospitalizations and emergency room visits
- Mortality (Asthma-specific and total)
- Use of oral steroids including a reduction in dose for those on chronic oral steroids
- Peak flow
- Forced expiratory volume in 1 second (FEV₁)
- Absence from school
- Absence from work
- Symptom scale/quality of life including nocturnal symptoms

Timing

Evidence on intervention effectiveness and harms will be derived from studies of any duration.

Settings

All relevant settings will be considered, including inpatient, clinic, and outpatient settings.

Simulation Models:

We will develop a simulation model to assess the cost-effectiveness of mepolizumab added to high-dose inhaled corticosteroid therapy and at least one additional controller medication relative to daily inhaled corticosteroid and other controller therapy alone. Model structure will be based on a previously-published long-term model of severe asthma conducted from the health-system perspective.⁴ Key model outputs will include exacerbations (including oral steroid “bursts”, emergency room visits, and hospitalizations), requirements for chronic oral steroid use, asthma-related mortality, and the impact of these events on health-related quality-of life. Costs will include those of treatment (including office visits where applicable), exacerbations, and ongoing chronic asthma care. Results will be expressed primarily in terms of the cost per quality-adjusted life year (QALY) gained.

We will also assess the budgetary impact of mepolizumab over a 5-year time horizon, utilizing information on treatment costs and cost offsets from reduced rates of exacerbation. Budgetary impact analyses will assume a specific product “uptake” rate over the 5-year period. Finally, we will develop a “value-based price benchmark” for mepolizumab; this benchmark represents a “policy trigger” for managing the cost of new interventions with a budgetary impact that exceeds the level of growth in the overall US economy.

More information on ICER’s methods for estimating product uptake and calculating value-based price benchmarks can be found at: <http://www.icer-review.org/wp-content/uploads/2014/01/Slides-on-value-framework-for-national-webinar1.pdf>.

References:

1. Centers for Disease Control and Prevention. Asthma Facts—CDC's National Asthma Control Program Grantees. 2013.
2. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. *The Journal of allergy and clinical immunology*. 2007;120(5 Suppl):S94-138.
3. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *The European respiratory journal*. 2014;43(2):343-373.
4. Campbell JD, Spackman DE, Sullivan SD. The costs and consequences of omalizumab in uncontrolled asthma from a USA payer perspective. *Allergy*. 2010; 65:1141–1148.