CHEST Medicare Drug Price Negotiation Program Information Collection Request Survey Response

CHEST submitted organizational comments in response to Centers for Medicare and Medicaid Services' (CMS) Information Collection Request regarding drugs primarily utilized in pulmonary, critical care, and sleep medicine that are under analysis within the third cycle of negotiations for the Medicare Drug Price Negotiation Program.

CMS' Questions Regarding Clinical-focused Experience with Xolair:

Questions: Clinical-Focused Experience

Question 1: Treatment-related Questions
What are goals of treatment for the condition(s) treated by Xolair?

- Examples of treatment goals may include but are not limited to disease remission, symptom management, quality of life improvement, or cure.

Response
The goals of treatment for asthma by Xolair include reduced frequency and severity of asthma attacks, improved lung function and breathing, decreased exacerbations and reliance on oral corticosteroids, reduced emergency room visits and hospitalizations, and improved daily activity tolerance and overall symptom control.

Question 2: What outcomes do you use to assess improvement or treatment response for this indication(s)?

- Please provide specific clinical, functional, or patient-reported outcomes.

Response

The outcomes used to assess improvement or treatment response are inclusive of clinical, functional, and patient-reported outcomes.

Clinical outcomes often assessed include a reduction in asthma exacerbations, fewer oral corticosteroid bursts, fewer ER visits/hospitalizations, decreased rescue inhaler use (SABA frequency), and reduction in maintenance oral corticosteroid dose.

Functional outcomes often assessed include FEV1 improvement (spirometry), Peak Expiratory Flow (PEF), Pulmonary Function Tests (PFTs), and reduced airway hyperresponsiveness.

Patient-reported outcomes often assessed include the Asthma Control Test (ACT) score, the Asthma Control Questionnaire (ACQ), rate of nighttime awakenings, activity limitation, and quality of life utilizing the Asthma Quality of Life Questionnaire (AQLQ).

Question 3: What would you consider to be a meaningful improvement or treatment response for the outcomes listed in Question 41b?

Response
For patients with asthma, meaningful improvement or treatment response includes reduction in asthma exacerbations, ideally approaching 50-60% reduction. This would be evidenced by less use of outpatient steroids, reduced ER or urgent care presentations, reduced admission to hospital. Additionally, meaningful improvement can include improved metrics of control of asthma, such as requiring less use of short-acting bronchodilators.

Question 4: Would you assess improvement or treatment response differently in certain patient subpopulations? If so, which subpopulations and why?

Response
Yes, in children, response assessment often emphasizes exacerbation reduction, school attendance, and caregiver-reported symptom control. In elderly patients or those with asthma–COPD overlap, functional status and exacerbation frequency may be more meaningful than changes in FEV_1. For patients with severe steroid-dependent asthma, the key outcome is the ability to safely reduce or eliminate maintenance oral corticosteroids while maintaining control. In obesity-associated asthma, symptom scores (e.g., ACT), activity tolerance, and exacerbation reduction may better reflect benefit than spirometric gains. Overall, assessment is individualized, with priority given to clinically meaningful reductions in exacerbations, oral steroid requirements and improvements in daily functioning.

Question: Additional Treatment-related Questions

Question 5: How does Xolair fit into the current treatment paradigm for patients with the conditions(s) treated by Xolair?

Response
Xolair is utilized for patients with severe persistent allergic asthma as an add-on therapy at Step 5/6 in stepwise asthma management, for patients with confirmed allergic (IgE-mediated) asthma, for patients with inadequate control on high-dose inhaled corticosteroid (ICS) and inhaled LABA, as evidenced by frequent exacerbations.

Question 6 What medications would you consider to be potential therapeutic alternatives for Xolair for treatment of the condition(s) treated with Xolair? For the list of potential therapeutic alternatives and indications, provide a brief explanation of the reason for the identification of the potential therapeutic alternative(s) of Xolair and any indication(s). Reference any citations listed where applicable.

Response
While considerations for therapeutic alternatives depend on a variety of factors including access and cost, potential therapeutic alternatives to Xolair include other broader biologics (e.g., anti-IL-5, anti-IL-4/13 agents such as Dupilumab and Tezepelumab). If a patient has an eosinophilic component in association with allergic asthma, then they may also respond to treatment with Mepolizumab, Benralizumab, or Depemokimab.

Question 7: What considerations drive treatment selection among Xolair and its potential therapeutic alternative(s) for the indication(s)?

- For example, relative efficacy, safety profile, route of administration, patient characteristics, patient preferences, cost, formulary placement, etc.

Response
While considerations for treatment selection depend on a variety of factors, Xolair is often selected when a patient's allergic trigger is a dominant driver of their symptoms and when eosinophils are not markedly elevated. Additionally, the availability of safety data, particularly for use during pregnancy, provides a differentiating characteristic when selecting Xolair (e.g. The EXPECT registry included more than 250 women that received at least one dose of Xolair).

Question 8: Are there notable differences between how Xolair or the potential therapeutic alternative(s) identified in question 6 are prescribed or managed in your practice setting and how these drugs are used in broader clinical practice and/or treatment recommendations in current clinical guidelines for the condition(s) treated with Xolair?

- For example, are there general debates or uncertainties related to selection or use of these drugs for the indication(s)?

Response
Yes, although Xolair is well established, there are ongoing clinical debates and areas of uncertainty regarding patient selection, positioning among biologics, duration of therapy, and cost-effectiveness across its indications. Additional notable differences include existing dosing intervals. Xolair requires a specific weight and IgE level with variable dosing that fluctuates between every two weeks to every four weeks. Other biologics use four weeks, eight weeks and up to six months for dosing intervals.

Question 9: How would you characterize the benefits and risks associated with Xolair?

Response
Xolair (omalizumab) has a well-established efficacy and safety record across allergic asthma, chronic spontaneous urticaria (CSU), chronic rhinosinusitis with nasal polyps (CRSwNP), and IgE-mediated food allergy. Overall, it is generally well tolerated and considered a clinically meaningful, steroid-sparing biologic with a favorable long-term safety profile, though cost and rare hypersensitivity reactions are key considerations. Benefits of reduced asthma exacerbations, reduced steroid requirements and improved asthma related quality of life and lung function are significant for patients. Protocols for dosing the first 1-3 doses under observation in outpatient setting and with EpiPen available are employed to reduce risk of hypersensitivity reactions with Xolair.

Question 10: What side effects or risks, common or serious, or other safety concerns would you take into consideration when selecting a treatment option from among Xolair or its potential therapeutic alternative(s) for the condition(s) treated with Xolair?

Response
There is a risk of anaphylaxis with Xolair, requiring patients to have an EpiPen. The required clinic visits for injections can be an added cost burden or barrier for patients. Many clinics have well established protocols which allow the first 1-3 doses to be monitored in an outpatient clinic setting, with dosing thereafter transitioning to patient administered home dosing.

Question 11: In your opinion, how do the benefits and risks associated with Xolair differ from the benefits and risks associated with its potential therapeutic alternative(s) for the indication(s)?

Response
While there are other biologics available for severe asthma, Xolair carries some specific labelling for IgE mediated food allergies and chronic spontaneous urticaria. Selection of biologics in asthma is nuanced and lacks head-to-head evidence base for guidance, but there are some guidelines that provide guidance in the choice of biologics. Generally, the benefits of biologics in asthma are to

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reduce exacerbations, but Xolair also carries data to improve asthma related quality of life. Selection of the right biologic for the right patient optimizes these benefits. Not every biologic will be appropriate for every patient, based upon their inflammatory profile (see below for specific populations).

Question 12: What specific populations or patient subgroups may derive greater benefits or be at risk for greater harms by using Xolair or any of its potential therapeutic alternative(s) for the indication(s)?

Response
The specific populations that Xolair is highly effective for include patients with severe allergic asthma, chronic urticaria, chronic rhinosinusitis with nasal polyposis, patients with food allergies, and pregnant patients with asthma. The specific populations that Xolair is less effective for include patients with low T2 asthma, patients with a history of hypersensitivity, and patients with mixed profile asthma.

Question 13: How would you assess whether a patient is tolerating and/or responding to Xolair or any of its potential therapeutic alternative(s) when used for each indication(s)?

- When might you consider discontinuing a medication?
- When might you consider switching to a different medication?
- When might you consider adding another medication to the regimen?

Response
Patient response to treatment with Xolair is assessed using patient symptoms and/or side effects. *A patient is considered responding well to treatment with Xolair if they exhibit a clinically meaningful reduction in asthma exacerbations, reduced systemic steroid exposure, improved lung function or asthma control, and acceptable tolerability without serious adverse events. If benefit is modest or unclear, clinicians will typically reassess phenotype and consider therapeutic alternatives—again speaking to the necessity to match the correct biologic with the correct patient in asthma.*

Question: Access and Patient Experience

Question 14 What health insurance coverage or access issues do patients experience when trying to obtain Xolair and its potential therapeutic alternative(s) for the condition(s) treated by Xolair?

Response
The variability and inconsistency in insurance coverage for Xolair and its potential therapeutic

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alternatives drives uncertainty and often results in suboptimal treatment options for patients with asthma due to financial burden. Common patient experiences include documentation-heavy processes, wherein approval is possible but administratively complex. Administrative barriers include complications with prior authorization that result in delayed treatment for patients, that is then further complicated by reauthorization which often requires documentation of specific measurable response to treatment. The required clinic visits for injections and the cost of EpiPens can also be an added access barrier and cost burden for patients.

Question: Therapeutic Advance and Unmet Medical Need

Question 15: For the condition(s) treated by Xolair, describe the extent to which Xolair currently represents (or does not represent) a therapeutic advance as compared to its potential therapeutic alternative(s).

Response
Xolair represents a foundational therapeutic advance that remains clinically important, though its relative distinctiveness has narrowed as additional biologics have entered the market. Xolair remains highly valuable in clearly IgE-driven disease and has shown to be well-tolerated by many subsets of patients since its initial approval. The current long-term safety data which is much more well established than the newer therapeutic alternatives—approved as recently as December 2025--and particularly for pregnant patients, is a significant strength of Xolair.

Question 18: What other information about Xolair, its potential therapeutic alternative(s), or the indication(s) do you think CMS should consider in its evaluation of Xolair? Reference any citations when applicable.

Response
CMS should consider several additional factors when evaluating Xolair across its indications (allergic asthma, CSU, CRSwNP, and food allergy): *1. Comparative positioning within the biologic class: Xolair is one of several biologics in asthma and CRSwNP; value depends on phenotype (e.g., clearly IgE-driven disease) and how it compares with pathway-specific alternatives.* *2. Patient selection and continuation criteria: Because predictive biomarkers are limited, coverage policies should emphasize documented clinical response (e.g., exacerbation reduction, steroid-sparing, validated symptom scores) rather than lab thresholds alone.* *3. Safety-related administration requirements: The anaphylaxis risk influences monitoring, site-of-care decisions, and cost under Medicare.* *4. Medicare benefit design (Part B vs Part D): Differences in reimbursement and cost-sharing for provider-administered vs self-administered therapy can materially*

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affect access and adherence. *5. Biosimilar impact: Availability of omalizumab biosimilars may change cost-effectiveness and formulary considerations. Overall, CMS should evaluate not only clinical efficacy, but also real-world access, phenotype-specific value, durability of response, and equity implications.*

Question 41c: Are there widely used evidence-based clinical practice guidelines for the condition(s) treated by the selected drug? If so, please cite these guidelines and explain how they are used to support clinical decision-making. For off-label use, please also reference any citations listed in Question 56 for major drug compendia, authoritative medical literature, and/or accepted standards of medical practice.

Response
Yes, the American College of Chest Physician guideline is used to support decision-making between various biologics depending on patient characteristics (Biologic Management in Severe Asthma for Adults, Oberle, Amber J. et al., CHEST, Volume 169, Issue 2, 336 – 348). *Additionally, the Global Asthma Initiative (GINA) guidelines are used to provide guidance for when to use each medication (Global Asthma Initiative, Difficult to Treat & Severe Asthma in Adolescent and Adult Patients, V6.0, 2025.)*