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REVIEW

Biologic Therapies in Pediatric Asthma: A Clinical Review of Current Advances

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ABSTRACT

Asthma is one of the most common chronic respiratory diseases in children and affects approximately 6%–7% of the global pediatric population. Despite advances in standard therapies such as inhaled corticosteroids and bronchodilators, a substantial subset of children continues to experience severe, uncontrolled disease that impairs quality of life and increases morbidity. The advent of biologic therapies targeting specific inflammatory pathways has transformed the management of severe pediatric asthma over the past two decades. This review summarizes the current evidence regarding biologic agents approved for pediatric use, including omalizumab, mepolizumab, dupilumab, and benralizumab. We discuss their mechanisms of action, clinical efficacy, safety profiles, and patient selection criteria. Evidence indicates that these targeted therapies can markedly reduce exacerbation frequency, improve lung function, and reduce corticosteroid dependence in appropriately selected patients. Persistent challenges include precise phenotyping, long-term safety monitoring, and limited accessibility owing to cost. Future research should emphasize biomarker-guided treatment strategies and their real-world effectiveness across diverse pediatric populations.

Keywords: Biologic therapy, omalizumab, pediatric asthma, severe asthma.

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1. Introduction

Asthma represents a significant public health burden in childhood, affecting an estimated 262 million individuals globally, with children comprising a substantial proportion of the population [1]. Pediatric asthma often presents with recurrent episodes of breathlessness, chest tightness, coughing, and wheezing, particularly at night or early in the morning [2]. Its heterogeneous nature, encompassing multiple phenotypes and endotypes, has reshaped our understanding of disease mechanisms and guided the evolution of precision-based treatment strategies. Standard management follows a stepwise approach using inhaled corticosteroids (ICS) and bronchodilators as foundational therapies [3]. However, approximately 5%–10% of children exhibit severe, uncontrolled asthma that remains poorly managed despite adherence to high-dose ICS and adjunctive controllers [4]. These children experience frequent exacerbations, hospitalizations, and diminished quality of life, while long-term corticosteroid exposure poses risks such as growth suppression and bone demineralization [5].

The recognition that asthma inflammation arises from distinct immunological pathways has led to the development of targeted biologic therapies. These monoclonal antibodies selectively inhibit mediators of type 2 (T2) inflammation, especially immunoglobulin E (IgE), interleukin-5 (IL-5), and interleukin-4/13 (IL-4/13) signaling [6], [7]. Over the past two decades, several biologics, including omalizumab, mepolizumab, dupilumab, and benralizumab, have gained approval for use in pediatric patients, representing a paradigm shift in the management of severe asthma. This review summarizes the current evidence on the mechanisms, efficacy, safety, and clinical applications of biologic therapies in children with asthma, emphasizing the importance of individualized treatment guided by disease phenotype and biomarker profile.

2. Overview of Biologic Agents

The current landscape of biologic therapy for pediatric asthma includes four approved monoclonal antibodies,

TABLE I: Comparison of FDA/EMA-Approved Biologic Therapies for Pediatric Asthma

Biologic agent/Molecular target	Mechanism of action	Approved age (years)	Dosing schedule	Key biomarkers	Primary efficacy outcomes
Omalizumab (Anti-IgE)	Binds circulating IgE, preventing mast-cell and basophil activation	≥6	SC every 2–4 weeks (weight- and IgE-based dosing)	Elevated total IgE (30–700 IU/mL) and positive allergen-specific IgE or skin test	Reduced exacerbations, improved asthma control, decreased corticosteroid use
Mepolizumab (Anti-IL-5)	Neutralizes IL-5, reducing eosinophil production and survival	≥6	SC every 4 weeks (40 mg for 6–11 yrs; 100 mg for ≥ 12 yrs)	Blood eosinophils ≥ 150 cells/μL (or ≥ 300 cells/μL in some studies)	Reduced severe exacerbations, lower oral corticosteroid requirement
Dupilumab (Anti-IL-4Rα)	Blocks IL-4 and IL-13 signaling, suppressing type 2 inflammation	≥6	SC every 2 weeks (weight-based 100 mg or 200 mg)	Elevated eosinophils and/or FeNO; evidence of type 2 inflammation	Reduced exacerbations, improved FEV_1, enhanced asthma control
Benralizumab (Anti-IL-5Rα)	Binds IL-5 receptor α on eosinophils, inducing depletion via ADCC	≥12	SC every 4 weeks × 3 doses, then every 8 weeks	Blood eosinophils ≥ 300 cells/μL	Reduced exacerbation rate, decreased oral corticosteroid dependence

Note: ADCC = antibody-dependent cell-mediated cytotoxicity; SC = subcutaneous; IgE = immunoglobulin E; IL = interleukin; FeNO = fractional exhaled nitric oxide; FEV_1 = forced expiratory volume in 1 second.

each targeting distinct elements of the type 2 inflammatory cascade (Table I). These biologics—omalizumab, mepolizumab, dupilumab, and benralizumab—have transformed the management of severe asthma by enabling precision treatment based on underlying inflammatory mechanisms.

2.1. *Omalizumab (anti-IgE)*

Omalizumab was the first biologic approved for pediatric asthma and has been the most extensively studied drug in children. A humanized monoclonal antibody that binds circulating IgE prevents its interaction with high-affinity receptors on mast cells and basophils, thereby attenuating allergic airway inflammation [8]. This medication is approved for children aged ≥6 years with moderate-to-severe allergic asthma. Omalizumab has consistently reduced the exacerbation frequency and improved control. The pivotal ICATA trial demonstrated significant reductions in seasonal exacerbations among inner-city children [9], with long-term studies confirming sustained efficacy and favorable safety. The dosing is weight- and baseline-IgE–based, administered subcutaneously every 2–4 weeks.

2.2. *Mepolizumab (anti-IL-5)*

Mepolizumab targets interleukin-5, a cytokine critical for eosinophil differentiation and survival, leading to marked eosinophil depletion and reduced airway inflammation [10]. It significantly lowers exacerbation rates and facilitates the tapering of oral corticosteroids in children aged ≥6 years with severe eosinophilic asthma. Pediatric studies have shown improvements in asthma control and quality of life, with weight-based subcutaneous dosing every 4 weeks.

2.3. *Dupilumab (anti-IL-4Rα)*

Dupilumab blocks the interleukin-4 receptor α subunit, thereby inhibiting both the IL-4 and IL-13 signaling pathways that drive IgE synthesis, eosinophilic inflammation, and airway remodeling [11]. Indicated for children aged ≥6 years with moderate-to-severe type 2 asthma, dupilumab improves lung function, reduces exacerbations, and benefits patients with comorbid atopic dermatitis or chronic rhinosinusitis. It was administered subcutaneously every 2 weeks.

2.4. *Benralizumab (anti-IL-5Rα)*

Benralizumab binds to IL-5 receptor α on eosinophils and basophils, inducing nearly complete cell depletion through antibody-dependent cytotoxicity [12]. Adolescents aged ≥12 years with severe eosinophilic asthma demonstrated substantial reductions in exacerbation frequency and oral corticosteroid dependence. Its dosing regimen—every 4 weeks for the first three doses, then every 8 weeks—offers practical advantages for long-term adherence.

Table I summarizes biologic therapies currently approved by the FDA and/or EMA for pediatric asthma, highlighting their molecular targets, mechanisms of action, age indications, dosing regimens, key biomarkers for patient selection, and principal clinical efficacy outcomes from randomized trials and real-world studies.

3. Discussion

3.1. *Patient Selection and Biomarkers*

The success of biologic therapy in pediatric asthma depends critically depends on the appropriate patient selection. In children aged 6 years or older with severe asthma that remains uncontrolled despite high-dose inhaled corticosteroids (ICS) and long acting beta agonist therapy (LABA) therapy, biologic selection should be guided by

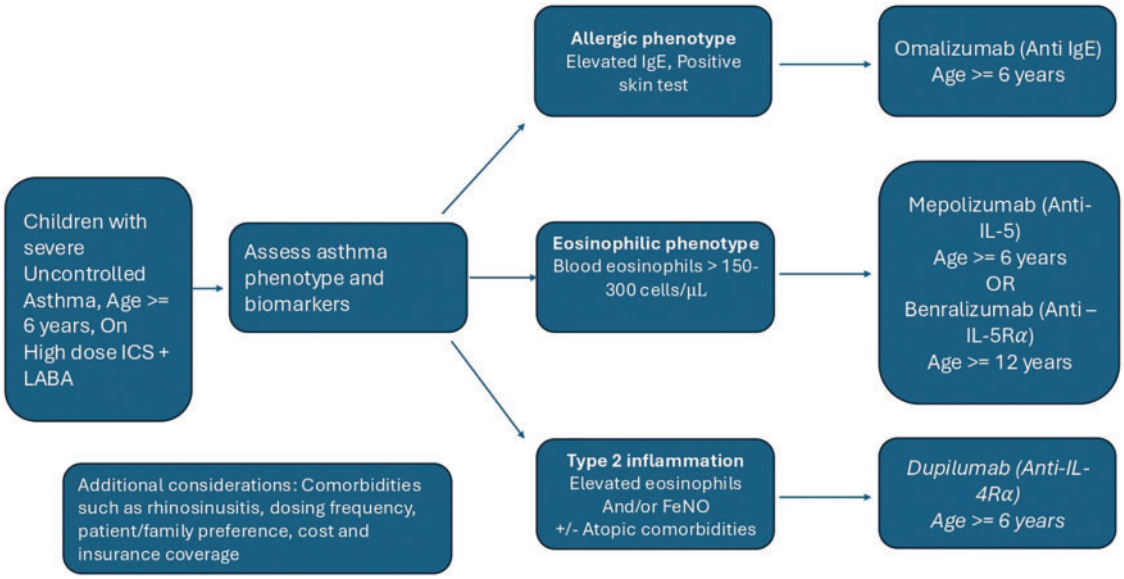

Fig. 1. Flowchart illustrating patient eligibility for biologic treatment in pediatric asthma. ICS=inhaled corticosteroids; LABA = Long-Acting Beta Agonist; IgE = Immunoglobulin E; IL = Interleukin; FeNO = Fractional Exhaled Nitric Oxide.

phenotype (Fig. 1). For omalizumab, total serum IgE levels and allergen-specific IgE sensitization remain essential selection criteria [8]. Mepolizumab and benralizumab require evidence of eosinophilic inflammation, typically defined as blood eosinophil counts ≥150–300 cells/μL, depending on the study and guideline [10], [12], [7]. Dupilumab demonstrates efficacy across a broader spectrum of type 2 (T2) biomarkers, including elevated levels of eosinophils, fractional exhaled nitric oxide (FeNO), and IgE [11], [7].

The concept of treatable traits has gained prominence in the management of severe asthma, emphasizing the need to address modifiable contributors before escalating to biologic therapy. Factors such as poor medication adherence, incorrect inhaler technique, persistent allergen or irritant exposure, and comorbidities, including rhinitis, gastroesophageal reflux, and obesity, can mimic treatment-resistant disease [13]. A systematic evaluation of these elements is essential before initiating costly biologic therapies.

3.2. *Safety Considerations in Children*

Safety remains paramount when novel therapies are introduced into the pediatric populations. Accumulated evidence from randomized trials and long-term extensions indicates that currently approved biologics exhibit favorable safety profiles in children and adolescents [8]–[12]. The most common adverse effects include injection-site reactions, headache, and nasopharyngitis, while serious events are rare and comparable to those of placebo.

However, several considerations warrant further attention. The long-term effects of sustained immune modulation during the critical growth and developmental periods remain unclear. Post-marketing registries and real-world surveillance are vital for detecting rare or delayed adverse events [7]. Although biologics may theoretically alter host defenses, clinical data have not demonstrated increased infection rates. Immunogenicity, although possible, is uncommon due to the humanized or fully human monoclonal antibody structure of these agents.

3.3. *Economic and Access Considerations*

The high cost of biologic therapies poses a significant barrier to equitable access in pediatric asthma care. Annual treatment expenses typically range from USD 30,000 to USD 40,000 per patient, varying by agent and dosing frequency [14]. Cost-effectiveness analyses suggest that biologics are economically justified for severe asthma when reductions in exacerbations and hospitalizations are considered. However, affordability challenges persist within many healthcare systems. Insurance coverage also varies widely, with prior authorization requirements, step therapy mandates, and restrictive eligibility criteria often delaying the initiation of appropriate therapy. Addressing these disparities is crucial to ensure equitable access to life-changing treatments for all children with severe asthma, irrespective of their socioeconomic background.

3.4. *Limitations and Future Directions*

Several limitations constrain the current study. Most randomized controlled trials have involved relatively homogeneous populations, leading to underrepresentation of diverse racial, ethnic, and socioeconomic groups [7], [13]. Moreover, direct head-to-head comparisons between biologics are lacking, limiting the precision of therapeutic decision-making. Future research should prioritize the validation of predictive biomarkers to guide initial biologic selection, assessment of combination or sequential biologic therapy for refractory disease, and evaluation of these agents in younger children. Longitudinal studies examining whether early biologic intervention can modify disease trajectory and prevent airway remodeling will be critical in defining the next frontier of pediatric asthma management.

4. Conclusion

Biologic therapies have transformed the management of severe pediatric asthma by providing targeted options for children who remain uncontrolled with standard therapy. The four approved agents, omalizumab, mepolizumab, dupilumab, and benralizumab, offer distinct mechanisms that reduce exacerbations, improve quality of life, and lower corticosteroid dependence in appropriately selected patients. Effective use demands precise phenotyping, confirmation of adherence and modifiable triggers, and alignment with patient-specific factors such as age, comorbidities, and preferences. Although the current evidence supports their efficacy and safety, long-term outcomes and equitable access remain key challenges. Future efforts should emphasize on validated biomarkers, early intervention, and real-world studies in diverse populations.

As the understanding of asthma endotypes deepens, emerging biologic targets promise to further personalize and improve care for children with severe asthma. Collaboration among clinicians, researchers, and policymakers is vital for translating these advances into accessible, sustainable care models. Ultimately, integrating biologic therapy into comprehensive, multidisciplinary asthma management offers the best opportunity to improve lifelong respiratory health in affected children.

Conflict of Interest

The authors declare that they do not have any conflict of interest.

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