REVIEW

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Biosimilars in allergology: an outline in pediatric patients

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Purpose of review
Biosimilars are increasingly shaping the management of pediatric allergic diseases and offering cost-effective alternatives to originator biology. This review summarizes the scientific and regulatory principles of biosimilars and examines the role of biosimilars in pediatric allergology, focusing on their clinical applications, opportunities, and challenges.

Recent findings
Biosimilars were developed through a stepwise comparability process, including analytical, pharmacokinetic, pharmacodynamic, and clinical evaluations, to ensure equivalence with reference products. Among pediatric allergies, biologics targeting type 2 inflammation have significantly improved outcomes in several diseases, including asthma, atopic dermatitis, chronic spontaneous urticaria, and food allergies. Omalizumab is currently the only biologic drug with an approved biosimilar that has demonstrated comparable efficacy, safety, and immunogenicity, even after switching. However, concerns remain regarding limited availability of long-term pediatric data.

Summary
Biosimilars represent a promising and sustainable opportunity to broaden access to advanced pediatric allergology therapies. Their integration into clinical practice, supported by growing evidence and appropriate clinical governance, has the potential to optimize treatment outcomes and improve long-term disease management. Further evidence on their risk–benefit profiles will help support their effective and informed use in the pediatric population.

Keywords
allergology, biosimilars, pediatrics, pharmacology

INTRODUCTION

Background

Scientific and regulatory foundations of biosimilarity

A biosimilar is a biological product highly similar to a U.S. Food and Drug Administration (FDA)-approved or EU European Medicines Agency (EMA)-approved reference product (originator), with no clinically meaningful differences in safety, purity, or potency despite minor variations in clinically inactive components. To establish biosimilarity, developers minimize uncertainty through analytical, preclinical, and clinical evaluations [1]. These include assessments of structural and functional properties, pharmacokinetic (PK) and pharmacodynamic (PD) profiles, and immunogenicity [2]. Biosimilars are evaluated for clinical safety and adverse events (AEs) to ensure efficacy and tolerability comparable to the reference product [3]. These studies were designed to detect clinically meaningful differences between the proposed biosimilar

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KEY POINTS

- Targeted biologics, small molecules, and biosimilars are transforming the management of pediatric allergic and immune-mediated diseases, enabling precise and effective disease control.
- Biosimilars offer a critical opportunity to enhance treatment accessibility and healthcare sustainability, supported by robust evidence of clinical equivalence and safety, including switching contexts.
- Pediatric-specific considerations, including developmental stage, long-term treatment exposure, and psychosocial factors, require tailored clinical, educational, and communication strategies.
- Structured clinical governance, active pharmacovigilance, and real-world data generation are essential to ensure long-term safety and optimize therapeutic outcomes.
- Transparent communication and shared decision-making are pivotal for minimizing nocebo effects, promoting adherence, and strengthening therapeutic alliances with patients and caregivers.

and the originator [4]. The U.S. framework is more prescriptive and trial-focused, often requiring at least one confirmatory comparative clinical study. By contrast, the EU process is more flexible, tailoring clinical requirements based on the strength of analytical and comparative data [5].

Benefits and challenges of biosimilar use in clinical practice

Biosimilars offer several advantages, including potential use across a wide spectrum of pathological conditions [6]. They also stimulate market competition, which can drive innovation in the development of next-generation biologics [7]. Furthermore, their lower cost compared to that of the originators represents a major advantage for healthcare systems. Although biosimilars are generally less expensive than originator biologics, their development cannot be equated with that of generic drugs because they are inherently more complex and require greater investment and longer development timelines [8].

Despite these advantages, their clinical use presents several challenges. Immunogenicity remains a critical concern because even minor manufacturing differences (i.e., variations in post-translational modifications such as glycosylation) may affect safety, efficacy, and overall clinical performance. This reinforces the need for rigorous quality control to limit immune responses [9]. Another important issue is interchangeability. Unlike the FDA, the EMA does not assign an interchangeability designation, leaving individual clinicians with the decision to switch from originators to biosimilars [10]. Finally, regulatory complexity remains a substantial barrier, as many countries are still developing approval frameworks and additional requirements (i.e., enhanced clinical monitoring and postmarketing surveillance), which further contribute to uncertainty around biosimilar adoption in clinical practice [11]. In many healthcare systems, cost-containment strategies encourage the use of biosimilars and may promote switching from the originator biologics [12], although clinical judgment remains essential, particularly in cases of reduced efficacy or AEs.

The broader advantages and challenges of biosimilars are particularly relevant in pediatric allergology, where the recent introduction of the first biosimilars requires careful evaluation of disease-specific needs and the robustness of supporting clinical and product data. Therefore, this review explores the role of biosimilars in pediatric allergology, focusing on their different possible clinical applications across allergic diseases in Europe, particularly in Italy, starting from already approved biologics and the therapeutic opportunities arising from their introduction, together with the technical and pharmacological attributes that guide their appropriate use.

Use of biologic therapies in pediatric allergy

Allergic diseases are immune-mediated conditions characterized by hypersensitivity and susceptibility to common antigens. They result from allergen-triggered immune activation, leading to inflammation, tissue damage, and chronic or acute clinical manifestations [13]. These conditions were developed in two stages. During sensitization, the immune system first encounters an allergen. In the second phase, inflammatory mediators are produced, leading to clinical manifestations [14]. Allergic disorders, including allergic asthma, allergic rhinoconjunctivitis (AR), atopic dermatitis (AD), and immunoglobulin E (IgE)-mediated food allergies (FA), cause significant morbidity in children and adults. Their prevalence and incidence have increased, with higher rates in younger populations and high sociodemographic index countries. In 2019, there were 262 million asthma cases and 171 million AD cases globally [15].

In patients unresponsive to conventional therapy, biologics targeting specific immune pathways have revolutionized the management of asthma, AD, chronic spontaneous urticaria (CSU), FA, chronic rhinosinusitis with nasal polyps (CRSwNP), eosinophilic gastrointestinal diseases (EGIDs), and AR [16▪▪].

Asthma

Asthma is a heterogeneous, chronic respiratory disease characterized by airway inflammation, mucus overproduction, variable airway obstruction, and progressive tissue remodeling [17▪]. Globally, over 300 million individuals are affected [18]. Severe asthma is estimated to affect approximately 3% of children [19,20]. Although mortality is rare, these patients remain at an increased risk of severe exacerbations and irreversible airway remodeling, increasing the risk of developing chronic obstructive pulmonary disease (COPD) in adulthood.

Biological therapies have emerged as targeted and effective treatments for severe or refractory asthma.

Currently, five biologics have been approved by the FDA and EMA for pediatric patients: omalizumab, mepolizumab, benralizumab, dupilumab, and tezepelumab (Table 1). These agents act on specific pathogenic mediators: omalizumab binds IgE; mepolizumab, reslizumab, and benralizumab target the interleukin (IL)-5 pathway, modulating eosinophil activation and reducing airway inflammation; dupilumab inhibits the IL-4 receptor α, shared by IL-4 and IL-13 signaling; and tezepelumab blocks thymic stromal lymphopoietin (TSLP), a master regulator of type 2 immune responses [21▪▪]. Reslizumab has also been approved for severe asthma, but only for adult patients. Among the novel biological therapies under investigation, depemokimab, lebrikizumab, tozorakimab, astegolimab, itepekimab, melrilimab, risankizumab, and ecleralimab have reached phases 2a, 2b, and 3 of clinical trials [16▪▪]. To date, all of these agents are available in Italy; however, only omalizumab is marketed in both originator and biosimilar formulations.

Atopic dermatitis

AD is a complex inflammatory skin disease characterized by severe pruritus, impaired epidermal barrier, and immune dysregulation [22,23]. It affects approximately 4% of pediatric patients and 2% of adults worldwide [24]. In 2024, the American Academy of Dermatology (AAD) recommended the use of topical treatments, particularly emollients, instead of phototherapy or systemic therapy [i.e., immunosuppression, corticosteroids, antimetabolites, Janus kinase inhibitors (JAK)] for severe cases [25]. Although several clinical phenotypes have been defined, no consensus exists on AD endotypes. Specific immune pathways, cytokines, and biomarkers have been identified. Despite this heterogeneity, T helper 2 (Th2)-driven inflammation, which is characterized by IL-4 and IL-13 production, plays a central role in the pathophysiology of AD [26].

Current guidelines for AD endorse a step-up approach, with topical anti-inflammatory therapies (corticosteroids and calcineurin inhibitors) as the first-line treatment in mild cases and systemic interventions for severe disease. Traditional systemic immunosuppressants (e.g., cyclosporine, methotrexate, mycophenolate, and azathioprine) and phototherapy have long represented the main options but are limited by safety concerns and inconsistent efficacy. Recently, targeted therapies, including biologics and JAK inhibitors (abrocitinib, baricitinib, and upadacitinib for systemic use, and ruxolitinib and delgocitinib for topical application), acting on key type 2 inflammatory pathways, have deeply transformed the therapeutic landscape of AD [27].

The FDA and EMA have approved four biologics for pediatric patients with moderate-to-severe AD: dupilumab, tralokinumab, lebrikizumab, and nemolizumab (Table 1). Tralokinumab and lebrikizumab neutralize IL-13, whereas nemolizumab blocks the action of IL-31, thus relieving disease manifestations.

Several biologics have been investigated for AD, including bermekimab, cendakimab, eblasakimab, stapokibart, rademikibart, itepekimab, astegolimab, melrilimab, ligelizumab, and rocatinlimab [16▪▪]. Among biologics for severe AD, dupilumab and tralokinumab are recommended by the AAD [25] and are available in Italy, along with lebrikizumab and nemolizumab. To our knowledge, no biosimilars have been developed for these biologics.

Chronic spontaneous urticaria

CSU is characterized by sudden wheals (hives), angioedema, or both for more than 6 weeks without external triggers and affects 1% of the global population [28,29]. Clinical manifestations of CSU are often caused by the activation of high-affinity IgE receptors on mast cells, releasing pro-inflammatory mediators, impacting patients' health-related quality of life (QoL), and causing socioeconomic burdens. Current guidelines recommend step-up administration of second-generation H1-antihistamines, followed by omalizumab and cyclosporine in refractory cases.

Currently, two biologics have been approved by the FDA and EMA for pediatric patients with symptomatic CSU despite H1 antihistamine treatment: omalizumab and dupilumab (Table 1). Moreover, ligelizumab, another high-affinity anti-IgE monoclonal antibody, has shown good tolerability and efficacy in patients with CSU in phase II and III clinical trials [30]. Finally, benralizumab and lirentelimab are under investigation for approval [16▪▪]. Even for CSU, omalizumab is the only agent marketed both as an originator and as a biosimilar in Italy.

Chronic rhinosinusitis with nasal polyps

CRSwNP affects 25–30% of patients suffering from chronic rhinosinusitis and 2–4% of adults [31,32].

Table 1. Pediatric indications and age thresholds for allergic disease biologics

Biologic	Target	Indications	Approved age	
			EMA	FDA
Omalizumab	IgE	Moderate-severe asthma in patients with a positive SPT or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids	≥6y	≥6y
		IgE-mediated food allergy	Not approved	≥1y
		Chronic spontaneous urticaria in symptomatic patients despite H1 antihistamine treatment	≥12y	≥12y
Mepolizumab	IL-5	Add-on maintenance treatment of patients with severe asthma and with an eosinophilic phenotype	≥6y	≥6y
		HES for ≥6 months without an identifiable nonhematologic secondary cause	≥18y	≥12y
Benralizumab	IL-5Rα	Add-on maintenance treatment of patients with severe asthma and with an eosinophilic phenotype	≥18y	≥6y
Dupilumab	IL-4Rα (blocks IL-4 and IL-13)	Add-on maintenance treatment of patients with severe asthma and with an eosinophilic phenotype or with oral corticosteroid dependent asthma	≥6y	≥6y
		Moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	≥6 months	≥6 months
		Eosinophilic esophagitis	≥1y (and ≥15 kg)	≥1y (and ≥15 kg)
		Chronic spontaneous urticaria in symptomatic patients despite H1 antihistamine treatment and who have not received medicines targeting IgE	≥2y	≥2y
		Add-on maintenance treatment in patients with inadequately controlled CRSwNP	≥18y	≥12y
		Allergic fungal rhinosinusitis in patients who have a history of sino-nasal surgery	Not approved	≥6y
Tezepelumab	TSLP	Add-on maintenance treatment of patients with severe regardless of eosinophilic status	≥12y	≥12y
		Add-on maintenance treatment in patients with inadequately controlled CRSwNP	≥18y	≥12y
Tralokinumab	IL-13	Moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	≥12y	≥12y
Lebrikizumab	IL-13	Moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	≥12 y (and ≥40 kg)	≥12 y (and ≥40 kg)
Nemolizumab	IL-31	Moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	≥12y	≥12y

AD, atopic dermatitis; CRSwNP: chronic rhinosinusitis with nasal polyps; HES: hypereosinophilic syndrome; IgE, immunoglobulin E; SPT, skin prick test; y, years.

CRSwNP typically presents with gradually worsening bilateral nasal obstruction, often accompanied by sinus pressure, facial fullness, increased mucus production, and thick nasal discharge. Olfactory dysfunction is also frequent, with up to 90% of the patients reporting a reduced (hyposmia) or absent (anosmia) sense of smell [33]. Management includes long-term intranasal corticosteroids, short-term systemic corticosteroids, and, in severe cases, surgical intervention. If the symptoms remain uncontrolled, biological therapies may be considered [34].

Currently only dupilumab and tezepelumab have been approved by FDA in pediatric patients $\geq$12 years old (Table 1). A phase 3 clinical trial (registration number NCT06338995) is currently investigating lebrikizumab efficacy (LY3650150) in participants with CRSwNP treated with intranasal corticosteroids aged $\geq$12 years [35]. Mepolizumab is currently approved by the FDA for CRSwNP in adults.

Eosinophilic gastrointestinal diseases

EGIDs are chronic, progressive, immune-mediated inflammatory disorders that can occur in both children and adults, and involve the esophagus, stomach, small intestine, and colon. Data regarding prevalence vary according to the specific disease: 34.4 per 100 000 people in North America and Europe for eosinophilic esophagitis (EoE) and 3–8 per 100 000 individuals for non-EoE [36]. Dietary modifications, proton pump inhibitors, corticosteroids, and budesonide may lead to the remission of EoE [37–39].

The only FDA- and EMA-approved biological treatment for children with EoE is dupilumab, but it is still not approved for EGIDs non-EoE (Table 1). Cendakimab, a high-affinity monoclonal antibody that binds IL-13, demonstrated improvements in the symptoms, histologic response, and endoscopic features of EoE in a phase III clinical trial involving adolescent and adult patients ($\geq$12 years) [40]. Moreover, dupilumab is also under investigation for non-EoE EGIDs, and benralizumab, mepolizumab, and reslizumab have been evaluated for EoE. To date, only dupilumab has been available as an originator.

Immunoglobulin E-mediated food allergy

FA is an immune-mediated adverse reaction to food. FA is classified as IgE-, non-IgE-, or mixed IgE/non-IgE-mediated based on IgE involvement in pathogenesis. IgE-mediated is a FA reaction occurring within 2 h of allergen exposure, reproducible upon re-exposure, with evidence of IgE sensitization and/or effector cell response to the allergen [41]. Although virtually any food can trigger an allergy, the major allergens responsible for the most significant reactions include milk, eggs, peanuts, tree nuts, shellfish, wheat, sesame, and soy [42].

Currently, omalizumab is the only biologic approved for children by the FDA for IgE-mediated FA, both as a monotherapy for the reduction of allergic reactions (Type I), including anaphylaxis, which may occur with accidental exposure, and under investigation as as a combination therapy with oral immunotherapy (OIT) to increase tolerance (Table 1). Several biologics are under clinical evaluation, particularly as adjuncts to OIT, to improve safety and expand the applicability of ligelizumab, reslizumab, lirentelimab, renalizumab, dupilumab, mepolizumab, and vedolizumab [16▪▪].

Allergic rhinoconjunctivitis

AR is an allergic disorder of the nose and eyes, resulting in chronic, mostly eosinophilic inflammation of the nasal mucosa and conjunctiva [43]. AR is one of the most common allergic diseases worldwide, affecting 400 million people. It significantly influences sleep quality, occupational, academic, and school performance, as well as leisure activities, and is frequently associated with asthma [44–46].

AR is usually diagnosed based on typical symptoms, including itching, sneezing, watery nasal discharge, and nasal congestion [43]. Although allergen avoidance is recommended, it is often impractical, leading to reliance on symptomatic pharmacotherapy, which does not alter disease progression and may cause adverse effects. In contrast, allergen immunotherapy (AIT) is the only treatment that modifies the natural history of allergic diseases [43,47].

Although no biologics have been formally approved solely for AR according to the EMA and FDA, omalizumab has shown efficacy in patients with AR, particularly in combination with AIT [48,49,50]. Additionally, dupilumab significantly alleviates AR-related symptoms, including nasal congestion, rhinorrhea, and sneezing, compared with placebo [51]. Among the novel biologics for AR, tezepelumab, stapokibart, and telikibart are undergoing phase 2 clinical trials in adults [16▪▪].

Omalizumab: originator and biosimilar efficacy and safety data

Pharmacological properties of omalizumab

Omalizumab is a humanized anti-IgE antibody that binds to the Cε3 domain of human free IgE, preventing its interaction with the high-affinity FcεRI receptor on mast cells and basophils, thereby downregulating receptor expression and attenuating allergic inflammation.

Pharmacodynamic effects include rapid suppression of free IgE levels, reduction of FcεRI expression, and downstream modulation of type 2 inflammatory pathways, translating into clinically meaningful reductions in exacerbation rates and symptom burden [52].

Following subcutaneous administration, omalizumab displays slow absorption, dose-proportional pharmacokinetics, and a terminal half-life of approximately 26 days, supporting dosing intervals of 2–4 weeks, with clearance primarily mediated through the reticuloendothelial catabolism of IgG–IgE immune complexes [53].

Omalizumab safety profile

Despite its established safety and tolerability, safety concerns with omalizumab have emerged since approval. Key concerns include anaphylaxis risk, pregnancy outcomes, and potential malignancies, cardiovascular complications, or infections [54]. Anaphylaxis has been reported in approximately 0.1–0.2% of patients, with a prior history of anaphylaxis identified as a risk factor [55]. Regarding pregnancy, data from the EXPECT study suggest that omalizumab exposure does not increase the risk of congenital anomalies or adverse birth outcomes compared with disease-matched cohorts [56]. While initial clinical trials raised theoretical concerns about malignancy, subsequent pooled analyses and the 5-year EXCELS study found no evidence of a causal relationship or a significant increase in cancer risk [57]. Similarly, although some data showed a higher crude incidence of serious cardiovascular and cerebrovascular AEs, further pooled analyses indicated that these rates were comparable to those of the control groups after accounting for baseline risk factors [58]. Finally, the risk of geohelminth infections remains a theoretical possibility because of the role of IgE in parasite defense, although current clinical evidence is insufficient to confirm a definitive link [59].

Clinical evaluation of originator and biosimilar omalizumab

The clinical efficacy and safety of omalizumab were established through pivotal randomized controlled trials in patients with moderate-to-severe allergic asthma and CSU, including both adult and pediatric populations, demonstrating significant reductions in exacerbation frequency, improved symptom control, and a favorable safety profile [60–63]. Long-term extension studies and postmarketing surveillance confirmed sustained efficacy, low immunogenicity, and acceptable safety profiles in children [64,65].

CT-P39 (omalizumab-igec) is the first omalizumab approved biosimilar. Its approval followed a rigorous stepwise comparability exercise, including extensive analytical characterization, pharmacokinetic and pharmacodynamic equivalence studies, and confirmatory clinical trials. To date, CT-P39 is approved for allergic asthma, CRSwNP, CSU, and (in the USA) IgE-mediated FA, and switching from reference omalizumab to CT-P39 appeared to have no impact on efficacy or safety [66].

In a randomized, double-blind, parallel-group phase 1 study conducted in healthy participants with total IgE $\leq$100 IU/ml, a single 150 mg subcutaneous dose of the proposed biosimilar CT-P39 demonstrated pharmacokinetic equivalence to both EU- and US-reference omalizumab. Equivalence was established for all primary pharmacokinetic endpoints (AUC_0–last, AUC_0–inf, and Cmax), with 90% CIs of geometric mean ratios fully contained within the predefined 80–125% equivalence margins. The pharmacodynamic responses, including a reduction in free IgE levels and an increase in total IgE serum concentrations, were comparable across the treatment groups. CT-P39 was well tolerated, with no treatment-related serious AEs, deaths, or discontinuations, and a safety and immunogenicity profile similar to that of the reference products [67].

In another randomized, double-blind, active-controlled phase 3 trial involving 619 patients with CSU, CT-P39 demonstrated therapeutic equivalence with the EU-approved reference omalizumab. At week 12, the primary endpoint-change from baseline in weekly itch severity score (ISS7)-confirmed equivalence between CT-P39 300 mg and reference omalizumab 300 mg, with treatment differences well within predefined equivalence margins (global analysis: 0.77, 95% CI –0.37 to 1.90; U.S. analysis: 0.70, 90% CI –0.22 to 1.63). Secondary efficacy outcomes, QoL measures, pharmacokinetics, and immunogenicity profiles were comparable across the treatment groups. Safety was similar, with no clinically meaningful differences in adverse event rates. Notably, no loss of efficacy, safety concerns, or immunogenicity signals emerged following switching from the reference product to CT-P39, supporting clinical interchangeability [68].

In an open-label, randomized phase 1 study conducted in healthy Japanese adults, CT-P39 administered via auto-injector demonstrated pharmacokinetic equivalence to EU-approved reference omalizumab delivered by prefilled syringe. Equivalence was confirmed for both primary pharmacokinetic endpoints, with geometric mean ratios (90% CI) of 101.66 (95.31–108.45) for AUC_0–inf and 93.91 (87.20–101.14) for Cmax, fully contained within the predefined 80–125% equivalence margins. The pharmacodynamic responses, safety, and immunogenicity profiles were comparable between the groups. Treatment-emergent AEs occurred in 60.0% and

50.8% of participants receiving CT-P39 and reference omalizumab, respectively, with no serious AEs reported, supporting the comparable tolerability of the two delivery systems [69].

In the 16-week off-treatment follow-up of a randomized, double-blind phase 3 trial in patients with CSU, CT-P39, and EU-approved reference omalizumab maintained comparable profiles in terms of efficacy, pharmacokinetics, pharmacodynamics, QoL, safety, and immunogenicity. Following treatment discontinuation at week 24, clinical improvement gradually declined but did not return to baseline levels, paralleling progressive reductions in serum omalizumab concentrations and normalization of total and free IgE levels. No clinically meaningful differences were observed between treatment groups across efficacy, QoL, safety, or immunogenicity outcomes, further supporting the sustained biosimilarity and clinical interchangeability of CT-P39 and reference omalizumab [70].

Conclusions: perspective in pediatrics

The expanding availability of targeted biologics, small molecules, and their biosimilar counterparts has profoundly reshaped the therapeutic landscape of pediatric allergic and immune-mediated diseases. These innovations have enabled earlier, more precise, and more effective disease control, with the potential to modify long-term disease trajectories and improve the QoL. Simultaneously, they introduced new clinical, organizational, and ethical challenges related to long-term safety, treatment selection, switching strategies, and healthcare sustainability.

In this evolving scenario, biosimilars represent a strategic opportunity to broaden equitable access to advanced therapies while ensuring economic sustainability. Robust clinical evidence supports their pharmacokinetics, pharmacodynamics, efficacy, and safety comparability with originator biologics, including switching settings. However, successful implementation in pediatric care requires structured clinical governance, careful pharmacovigilance, and proactive patient and caregiver engagement (Fig. 1).

Pediatric patients present with unique vulnerabilities and needs, including developmental considerations, long treatment horizons, and heightened sensitivity to contextual and psychosocial factors. Consequently, transparent communication, shared decision-making, and tailored educational strategies are essential to minimize nocebo effects, foster trust, and ensure optimal adherence.

Ultimately, the integration of biologics, biosimilars, and targeted small molecules into pediatric clinical practice should move beyond a purely pharmacological paradigm toward a comprehensive, patient-centered, and system-aware model of care. Long-term real-world evidence, pediatric-specific clinical studies, and multidisciplinary collaborations are crucial for refining treatment algorithms, optimizing outcomes, and ensuring sustainable innovation in pediatric allergology.

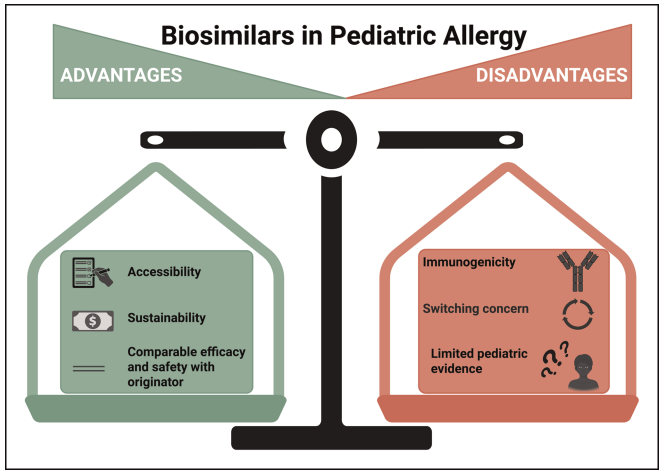

FIGURE 1. Biosimilars in pediatric allergy: advantages and disadvantages. Created with BioRender.com.

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- ■ of special interest
- ■■ of outstanding interest

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This review synthesizes recent findings and emerging trends, highlighting the evolving role of biologics in transforming allergic disease management and offering insights into future research directions.

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Asthma is a heterogenic and complex immune-mediated disease with inflammation at its core. Advancement in understanding about immunologic mechanisms involving contributions of Th2, Th1, and Th17 cells has substantially changed our treatment strategies. Targeted therapies against Type 2 inflammation, such as anti-IgE, anti-IL-5, and anti-IL-4/IL-13 therapies, have greatly improved outcomes of treatment in moderate-to-severe uncontrolled asthmatic patients despite conventional therapy.

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Asthma inherent heterogeneity has long challenged clinicians, as traditional anti-inflammatory and bronchodilator regimens fail to address the diverse immunological pathways underpinning severe disease. The advent of biologic therapies marks a paradigm shift, enabling direct interception of key molecular drivers, namely IgE, IL-5, IL-4, IL-13, IL-33, and TSLP, that orchestrate airway inflammation, remodeling, and exacerbations.

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