Quality in Sport eISSN 2450-3118 | apcz.umk.pl/QS Nicolaus Copernicus University in Toruń, Poland Unique Journal Identifier: 201398 | 20 pts — Ministry of Higher Education and Science of Poland

Quality in Sport. 2026;53:70169 eISSN 2450-3118 https://doi.org/10.12775/QS.2026.53.70169

FAHIM, Knieszko, FRANASZEK, Jakub, HERCHI, Nadia, JABRZYK, Martyna, JARCZYŃSKA, Patrycja, KIJOWSKI, Wojciech, KLUSEK, Mateusz, MICHALAK, Karolina and PRZYBYŁ, Maciej. Omalizumab usage off-label — review of the knowledge obtained over the last 10 years from research in specific diseases. *Quality in Sport*. 2026;53:70169. eISSN 2450-3118. https://doi.org/10.12775/QS.2026.53.70169

Received: 23.03.2026 Revised: 30.03.2026 Accepted: 30.03.2026 Published: 04.04.2026

Published by Nicolaus Copernicus University in Toruń, Poland | eISSN 2450-3118 | Unique Journal Identifier: 201398 | 20 pts (Ministry of Higher Education and Science of Poland, 05.01.2024, No. 32553)

Omalizumab usage off-label — review of the knowledge obtained over the last 10 years from research in specific diseases

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Abstract

Introduction: Omalizumab, a humanized monoclonal antibody binding to human Immunoglobulin E (IgE), limits free IgE triggering allergic reactions. Officially indicated for allergic asthma, chronic rhinosinusitis with nasal polyps, and chronic spontaneous urticaria, its off-label potential is gaining clinical interest. This spans common conditions such as atopic dermatitis to rare diseases such as systemic mastocytosis.

Aim of the study: To analyze knowledge from the last decade (2016–2026) on the off-label clinical efficacy of omalizumab in atopic dermatitis, IgE-mediated food allergy, latex allergy, systemic mastocytosis, and allergic bronchopulmonary aspergillosis (ABPA).

Materials and methods: A literature review of the PubMed database (2016–March 2026) was conducted using standardized search strings. Findings were supplemented by clinical guidelines and official drug characteristics from specialized medical textbooks and registries.

Conclusions: Omalizumab shows promising yet variable efficacy as an off-label therapy across IgE-mediated and inflammatory disorders. In food and latex allergies, it is a highly effective adjunct to oral immunotherapy, enabling safer, rapid desensitization. In cystic fibrosis patients with refractory ABPA, it yields consistent pulmonary (FEV1) and serological improvements. For atopic dermatitis, omalizumab significantly reduces severity in pediatric populations but is ineffective in adults with massively elevated IgE. In systemic mastocytosis, it prevents anaphylaxis in highly symptomatic patients, though trial results remain mixed. Ultimately, while offering substantial therapeutic potential, successful off-label application requires highly individualized, disease-specific dosing protocols rather than standard asthma nomograms.

Keywords: omalizumab; systemic mastocytosis; atopic dermatitis; food allergy; latex allergy; allergic bronchopulmonary aspergillosis

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Introduction

Omalizumab is a humanized monoclonal antibody produced by recombinant DNA technology from a Chinese hamster ovary cell line [1]. It is currently indicated for use in diseases such as IgE-induced allergic asthma, chronic rhinosinusitis with nasal polyps, and chronic spontaneous urticaria [2]. It is currently available under the trade name Omlyclo, manufactured by Celltrion, and under the name Xolair, manufactured by Novartis Europharm [3]. The mode of action of

omalizumab is to selectively bind to the C domain of epsilon 3 of human Immunoglobulin E (IgE), limiting the amount of free IgE that is responsible for triggering allergic reactions [4].

The book entitled *Allergology*, edited by Krystyna Obtułowicz and published in 2016, mentions the ongoing clinical trials of omalizumab in atopic dermatitis, IgE-dependent food allergy, latex allergy, mastocytosis, and bronchopulmonary aspergillosis [4]. The prospect of using omalizumab in therapy for the above-mentioned diseases for therapeutic or supportive purposes seems interesting, especially since we may be dealing with a drug with a broad therapeutic spectrum for diseases occurring very frequently in the general population, such as atopic dermatitis (2–8% of adults), and very rarely, such as mastocytosis (5–10 cases per 1,000,000) [5]. This study aims to analyze the knowledge obtained over the last 10 years from research on the use of omalizumab off-label in atopic dermatitis, IgE-dependent food allergy, latex allergy, mastocytosis, and bronchopulmonary aspergillosis.

Material and Methods

A literature review was conducted to evaluate the clinical applications and efficacy of omalizumab in various allergic and immunological disorders. The primary materials used for this study consisted of peer-reviewed scientific literature retrieved from the PubMed database (http://pubmed.ncbi.nlm.nih.gov/) in the time period from 2016 to March 2026. The PubMed database was queried using a standardized search string format: "omalizumab AND [term]", where [term] included: "systemic mastocytosis", "atopic dermatitis", "food allergy", "latex allergy", "allergic bronchopulmonary aspergillosis". In addition to the electronic database, foundational medical knowledge and clinical guidelines were sourced from two specialized medical textbooks: *Allergology* (ed. K. Obtułowicz, PZWL, 2016) and *Allergology. Specialist Manual* (Practical Medicine, 2024). Official drug characteristics were obtained from the European Commission and the Practical Medicine registry.

Omalizumab in Mastocytosis

Mastocytosis is a neoplastic disease characterized by excessive proliferation and accumulation of mast cells in one or more human organs. Oncotherapy is based on tyrosine kinase inhibitors (midostaurin, avapritinib), cladribine, and Peg-IFN-α [Pegasys], alone or in combination with GCS; in selected patients, allo-HCT is considered [18].

Samuel L. Weiss et al. describe a 32-year-old female patient with recurrent episodes of anaphylaxis at least 12 times a year, including 4 episodes of short-term loss of consciousness and recurrent urticaria. Despite maximal antihistamine and antileukotriene therapy with ranitidine, cetirizine, montelukast, and cromolyn sodium, therapy was initiated with subcutaneous injections of 300 mg of omalizumab every 4 weeks for more than 4 years. During this time, the patient experienced only one episode of anaphylaxis with noticeable improvement in skin symptoms. The authors concluded that omalizumab may be effective in the prevention of anaphylaxis and in the reduction of disease burden associated with systemic mastocytosis [6].

Calum Slapnicar et al. retrospectively analyzed data from 6 patients from their stay at St. Michael's from 2009 to 2018, diagnosed with indolent systemic mastocytosis treated with

omalizumab. To assess disease control, the incidence of anaphylaxis, baseline and control tryptase levels, and symptoms associated with the underlying disease were recorded.

A 28-year-old male patient with indolent systemic mastocytosis, c-kit D816V mutation, and serum tryptase of 134 ng/ml suffered from typical symptoms despite the use of sodium cromoglycate, ketotifen, and cetirizine. At the end of 2014, he underwent additional therapy with omalizumab at a dose of 150 mg every 4 weeks without a significant response; therefore, the dose of omalizumab was increased to 300 mg every 4 weeks (at the beginning of 2015), which after just 4 months achieved a reduction in tryptase levels from 134 ng/ml to 84 ng/ml with complete control of symptoms for 7 months. An attempt to reduce the dose of omalizumab to 150 mg every 4 weeks resulted in a return of episodic flushing, nausea, bone pain, palpitations, and diarrhea, as well as 2 anaphylactic reactions, both requiring hospitalization within 6 weeks. The basal tryptase concentration increased to 100 ng/ml. The dose of omalizumab was increased to 300 mg at 2-week intervals and then maintained at 4-week intervals. At the beginning of 2017, he had only one case of exacerbation of symptoms: facial flushing, dizziness, and diarrhea. In April 2018, 3 months after omalizumab injections had been discontinued, the patient reported his first anaphylactic reaction in nearly two years. The number of skin lesions of urticaria pigmentosa was not controlled by omalizumab, and later he required ultraviolet therapy with a good clinical response [7].

A 40-year-old female with indolent systemic mastocytosis presented with daily flushing, nausea, abdominal discomfort, and loose stools 3–4 times per day. Treatment with omalizumab 300 mg every 4 weeks was initiated. After 3 injections, GI symptoms had subsided. After 6 cycles of omalizumab, cutaneous lesions had decreased in number, daily palpitations and syncopal episodes had subsided. She was able to discontinue both ketotifen and cromolyn with ongoing treatment with omalizumab [7].

A 49-year-old woman was diagnosed with indolent systemic mastocytosis with a tryptase level of 11.4 ng/ml. She presented with most ISM symptoms except cutaneous manifestations. She was already treated with ranitidine, loratadine, cetirizine, ketotifen, and montelukast. Despite this, she experienced 5 anaphylactic reactions, requiring emergency department visits and treatment with epinephrine. Omalizumab was started at 300 mg at 4-week intervals. A follow-up one year later revealed complete resolution of symptoms, no adverse reactions to medications, and a reduction in tryptase to 8.3 ng/ml [7].

A 32-year-old male with indolent systemic mastocytosis suffered from daily diarrhea, numbness, and tingling sensation in his extremities, night sweats, severe headaches, and flushing upon strenuous physical activity. Because the symptoms were refractory to a combination of cetirizine, ranitidine, montelukast, and cromolyn, he was started on omalizumab 300 mg at 4-week intervals. A follow-up 8 months later revealed improved symptomatic control and a fall in tryptase from 42.2 to 34 ng/ml. However, he continued to experience intermittent itching, flushing, and diarrhea. A follow-up in late 2018 revealed that he had chosen to discontinue omalizumab, with continued control of disease [7].

A 72-year-old female was diagnosed with indolent systemic mastocytosis without cutaneous manifestations. Her initial presentation was that of Hymenoptera anaphylaxis, with flushing, palpitations, and loss of consciousness. She experienced occasional facial flushing, vomiting, lightheadedness, drenching night sweats, and bone pain, even though she was treated with cetirizine and ranitidine. Omalizumab was started at 300 mg every 4 weeks for 14 months,

followed by rush venom desensitization. Symptoms of her underlying indolent systemic mastocytosis resolved completely on ongoing omalizumab therapy [7].

The authors also describe a 51-year-old female with indolent systemic mastocytosis who started 300 mg omalizumab injections every two weeks. Until the 4th cycle her symptoms had improved, but after that cycle of omalizumab she experienced an immediate multisystem reaction with respiratory distress and tongue swelling. A fifth cycle was attempted but again resulted in a similar reaction, leading to discontinuation of omalizumab therapy [7]. The authors are aware that this study concerns a small group of patients; yet they suggest that omalizumab should be considered in highly symptomatic patients with indolent systemic mastocytosis [7].

Meike Distler et al. conducted a double-blind, placebo-controlled trial with sixteen patients randomized to receive either omalizumab (7 patients) or placebo (9 patients), dosed according to IgE level and body weight. The authors concluded that omalizumab was safe and showed a tendency to improve mastocytosis-related symptoms, in particular diarrhea, dizziness, flushing, and anaphylactic reactions. Improvements were also observed in allergic reactions, changes in major complaints, and wheal-and-flare reaction due to mechanical irritation (Darier's sign); however, the difference was not statistically significant [8].

Omalizumab in Atopic Dermatitis

Atopic dermatitis is a chronic inflammatory skin disorder that affects up to 2–8% of adults and 15–20% of children worldwide. Although the mainstay of treatment is topical corticosteroids and calcineurin inhibitors, the majority of patients do not achieve adequate control of their condition and require systemic treatment with steroids and immunosuppressants [5,19].

Susan M.H. Chan et al. examined the role of omalizumab in 62 children and young people with severe eczema over 24 weeks. The participants were divided into two groups. The first group was treated with omalizumab; the second group received placebo. Omalizumab reduced eczema severity and improved quality of life, with a concomitant reduction in steroid use. Treatment benefit became more apparent towards 24 weeks and persisted after treatment stopped [9].

Raed Alzyoud describes a 6-year-old patient with atopic dermatitis. Even though the patient was treated with cyclosporine, prednisolone, and tacrolimus for 2 years, his SCORAD index was 70/103. The author then describes the decision to initiate omalizumab treatment at a dose of 300 mg twice weekly, which led to a drop in the SCORAD index to 57/103 at 12 weeks and to 55/103 at 18 weeks, with good drug toleration. Omalizumab treatment also led to discontinuation of systemic steroids at 15 weeks of treatment [10].

Miroslav Nečas et al. present their experience with omalizumab in the treatment of 2 patients with severe atopic dermatitis and extremely elevated IgE levels.

The first patient was a 44-year-old female with AD for 26 years, who was also diagnosed with asthma, allergic rhinitis, and polyvalent inhalant and food allergy. Treatment with omalizumab at 450 mg every 2 weeks was initiated when cyclosporine was insufficient and the patient's condition worsened (SCORAD 55), with IgE levels rising to 48,526 IU/ml. The patient experienced discomfort for 2–4 days after each injection of omalizumab, but the treatment as a whole was well tolerated. Three months of treatment led to improvement (SCORAD 50, IgE level 47,035 IU/ml); however, 6 months of treatment led to deterioration with nocturnal pruritus

(SCORAD 78, IgE level 45,929 IU/ml). After 9 months, omalizumab treatment was discontinued due to worsening of the patient's condition (SCORAD 80, IgE elevation to 66,000 IU/ml) [11].

The second patient was a 47-year-old female with atopic dermatitis since early childhood, also diagnosed with bronchial asthma and pollen allergy. She was treated with cyclosporine, but her skin condition and pruritus were declining (SCORAD 45, IgE level 61,904 IU/ml). Omalizumab was introduced at a dosage of 450 mg every 2 weeks. After 3 months of treatment, the patient's condition worsened (SCORAD 50, IgE elevation to 105,000 IU/ml). After another 3 months, the IgE level decreased to 53,700 IU/ml; however, skin condition and pruritus continued to decline (SCORAD 64). After 9 months, omalizumab injections were discontinued due to lack of efficacy (SCORAD 73, IgE level 48,600 IU/ml) [11].

The authors concluded that in patients with extremely elevated IgE concentrations, the effect of omalizumab treatment is not convincing. They also proposed that the solution in such cases might be pre-treatment with immunoadsorption prior to omalizumab initiation [11].

Omalizumab in Latex Allergy

Natural rubber latex is obtained from the latex sap of *Hevea brasiliensis*. In this latex sap, 60 polypeptides capable of binding allergen-specific IgE were detected, 15 of which were thoroughly characterized and designated Hev b 1 through Hev b 15, respectively. Clinical manifestations of sensitization include all forms of IgE-mediated allergy [20].

Arianna Aruanno et al. describe a study of an 11-year-old boy who had a 5.0 mm wheal for the latex extract in skin prick tests, latex IgE of 5.10 U/ml, and recombinant latex allergens Hev b 6.01 and Hev b 6.02 both at 5.17 kUA/l. The patient was treated with 300 mg omalizumab per month. The patient did not report clinical symptoms after any accidental contact with latex. After 6 years, the patient's allergological evaluation was repeated to monitor possible changes in latex immunological and allergological features. Following omalizumab treatment, the authors observed a reduction in latex sensitization, confirmed by a decrease in latex-specific IgE test positivity [12].

Omalizumab in IgE-Mediated Food Allergy

Sandra Andorf et al. in their pilot study investigated whether omalizumab combined with immunotherapy benefited multi-food allergic patients. Participants were aged 4–15 years and diagnosed with multi-food allergies. Thirty-six of them underwent oral immunotherapy to 2–5 foods combined with omalizumab, while 12 received placebo. Omalizumab or placebo was administered subcutaneously for 16 weeks, with OIT starting at week 8. Treatment was stopped 20 weeks before the exit double-blind, placebo-controlled food challenge at week 36. Participants in the omalizumab group had a significantly lower median per-participant percentage of oral immunotherapy doses associated with any adverse events (27% vs. 68%). Adverse events in both groups were mostly gastrointestinal. The authors concluded that omalizumab improves the efficacy of multi-food oral immunotherapy and enables safe and rapid desensitization [13].

In the study by Alexandra Langlois et al., 90 participants (aged 6–25 years) received omalizumab for 20 weeks at monthly dosages of 16 mg/kg, 8 mg/kg, or placebo (3 groups in a 2:2:1 ratio). Omalizumab was administered at full dosage for a total of 12 weeks, with a progressive taper during the last 8 weeks [14]. Multi-food oral immunotherapy was initiated after a pre-treatment period of 8 weeks. According to the proposed immunological mechanism, after 3–5 years of food dosing, the immune response against the allergen diminishes, leading to prolonged remission and allowing the dose to be discontinued [15].

Josef Brandström et al. treated 23 participants (aged 12–19 years) with peanut allergy using omalizumab and oral immunotherapy. Peanut oral immunotherapy with omalizumab protection was initiated at 280 mg of peanut protein and increased every 2 weeks to 2,800 mg. All 23 patients reached the 2,800 mg maintenance dose in a median time of 10 weeks. Moderate/systemic allergic reactions were rare while receiving full-dose omalizumab. The authors concluded that omalizumab is an effective adjunctive therapy for initiation and rapid up-dosing of peanut oral immunotherapy, but adverse events become more frequent as omalizumab doses are decreased [16].

Omalizumab in Allergic Bronchopulmonary Aspergillosis

Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity syndrome caused by exposure to allergens of the fungus *Aspergillus fumigatus*, which colonizes the respiratory tract most often in patients with asthma, cystic fibrosis, or COPD associated with bronchiectasis. Treatment includes: prednisone and itraconazole, with or without GCS. Treatment efficacy is assessed by a reduction in symptoms and a reduction in total serum IgE concentration by ≥20% [21].

Giuseppe Fabio Parisi et al. report three male patients aged 17, 28, and 11 years, all with cystic fibrosis and bronchopulmonary aspergillosis.

The first patient was diagnosed with cystic fibrosis with a progressive reduction in FEV1 from 80% to 40% predicted. His treatment consisted of: airway clearance, insulin therapy for CF-related diabetes, rhDNase, inhaled corticosteroids, pancreatic enzymes, ursodeoxycholic acid, and vitamins. Bronchopulmonary aspergillosis was diagnosed when the patient was hospitalized for respiratory exacerbation (IgE level: 1,124 IU/mL). After initial therapy with prednisone followed by itraconazole failed to yield improvement, the patient was treated with subcutaneous omalizumab. After the second injection of omalizumab, FEV1 and symptoms began to improve. Eight weeks of therapy yielded the following results: FEV1 improved to 93% predicted and IgE level decreased to 363 IU/mL [17].

The second patient was also diagnosed with cystic fibrosis. His treatment regimen consisted of airway clearance, inhaled corticosteroids, pancreatic enzymes, ursodeoxycholic acid, vitamins, and antibiotics. His FEV1 decreased from 68% to 50% predicted. At this point, he was diagnosed with bronchopulmonary aspergillosis (IgE level: 1,105 IU/mL). Steroid and antifungal therapy yielded only a partial benefit in terms of a slight reduction in daily cough. Therefore, the patient was started on omalizumab injections. At week 8 of therapy, his clinical condition improved, FEV1 improved to 83% predicted, and total IgE level decreased to 301 IU/mL [17].

The third patient was diagnosed with cystic fibrosis, with FEV1 decreasing from 60% to 40% predicted in recent months. He required the same treatment regimen as the previous patient. He was diagnosed with bronchopulmonary aspergillosis (IgE level: 1,056 IU/mL). Steroid and antifungal therapy administered for one month did not yield improvement. Significant clinical improvement was achieved with omalizumab injections. After 8 weeks of therapy, his FEV1 improved to 68% predicted and total IgE decreased to 456 IU/mL. The authors concluded that omalizumab supports the safety and efficacy of therapy, with dosages and dosing frequency based on the patient's weight and initial IgE values, as recommended for asthma [17].

Results

Systemic Mastocytosis

Omalizumab administration in patients with systemic mastocytosis demonstrated varied clinical and serological outcomes [6,7,8]. While individual case reports generally indicated positive clinical responses and reductions in basal tryptase levels, a double-blind, placebo-controlled trial observed no statistically significant difference between the omalizumab and placebo groups regarding mastocytosis-related symptoms or allergic reactions [8]. Severe adverse events, including multisystem reactions, were recorded in isolated cases, leading to treatment discontinuation [7]. Data are summarized in Table 1.

Table 1. Clinical and Serological Outcomes of Omalizumab in Systemic Mastocytosis

Subject / Study	**Dosage Regimen**	**Duration**	**Clinical Outcome**	**Serum Tryptase (Baseline → Final)**
32-year-old female [6]	300 mg / 4 weeks	> 4 years	Positive: 1 anaphylaxis episode; noticeable skin improvement.	Not reported
28-year-old male [7]	Variable (150 mg to 300 mg / 2–4 weeks)	~4 years	Mixed: Symptom control at 300 mg/4 weeks. Exacerbations/anaphylaxis upon dose reduction or discontinuation. Skin lesions uncontrolled.	134 ng/ml → 84 ng/ml (at 300 mg); 100 ng/ml (upon dose reduction)
40-year-old female [7]	300 mg / 4 weeks	6 cycles	Positive: Subsidence of GI symptoms, palpitations, syncope; decrease in cutaneous lesions.	Not reported

Subject / Study	Dosage Regimen	Duration	Clinical Outcome	Serum Tryptase (Baseline → Final)
49-year-old female [7]	300 mg / 4 weeks	1 year	Positive: Complete symptom resolution; no adverse reactions.	11.4 ng/ml → 8.3 ng/ml
32-year-old male [7]	300 mg / 4 weeks	8 months	Positive/Mixed: Improved control; intermittent itching, flushing, diarrhea continued.	42.2 ng/ml → 34.0 ng/ml
72-year-old female [7]	300 mg / 4 weeks	14 months	Positive: Complete symptom resolution.	Not reported
51-year-old female [7]	300 mg / 2 weeks	5 cycles	Negative: Improvement until 4th cycle; immediate multisystem reaction (respiratory distress, tongue swelling) at 4th and 5th cycles. Treatment discontinued.	Not reported
16 patients (Trial) [8]	Dosed by IgE/weight	Not reported	Neutral: Tendency to improve symptoms, but difference from placebo was not statistically significant.	Not reported

Atopic Dermatitis

In pediatric populations, omalizumab demonstrated positive results by reducing eczema severity and lowering the requirement for systemic steroids [9,10]. Conversely, in adult patients with severe atopic dermatitis and extremely elevated baseline IgE levels, the clinical response was negative, characterized by progressive worsening of the SCORAD index and fluctuations in IgE concentrations, ultimately resulting in treatment cessation [11]. Data are summarized in Table 2.

Table 2. Omalizumab Efficacy in Atopic Dermatitis

Subject / Study	Dosage Regimen	SCORAD Index (Initial → Final)	IgE Levels (Initial → Final)	Clinical Outcome
62 children (Trial) [9]	Not reported	Not reported	Not reported	Positive: Reduced eczema severity, improved quality of life, reduced steroid use. Benefit persisted after 24 weeks.
6-year-old patient [10]	300 mg / 2× week	70/103 → 55/103 (at 18 weeks)	Not reported	Positive: Good toleration; systemic steroids stopped at 15 weeks.
44-year-old female [11]	450 mg / 2 weeks	55 → 80 (at 9 months)	48,526 IU/ml → 66,000 IU/ml (at 9 months)	Negative: Temporary improvement at 3 months, followed by deterioration and nocturnal pruritus. Treatment discontinued.
47-year-old female [11]	450 mg / 2 weeks	45 → 73 (at 9 months)	61,904 IU/ml → 48,600 IU/ml (at 9 months; peaked at 105,000 IU/ml at 3 months)	Negative: Declining skin condition and pruritus. Treatment discontinued due to lack of efficacy.

Latex and IgE-Mediated Food Allergies

Data indicate positive outcomes for the use of omalizumab as an adjunctive therapy or standalone treatment in specific allergies [12,13,16]. In multi-food and peanut oral immunotherapy (OIT), omalizumab was associated with a reduction in the percentage of doses causing adverse events and facilitated rapid up-dosing [13,16]. However, adverse events increased when omalizumab dosages were tapered [16]. Data are summarized in Table 3.

Table 3. Outcomes in Latex and Food Allergies

Condition	Subject / Study	Intervention	Clinical Outcome
Latex Allergy	11-year-old boy [12]	300 mg / month	Positive: No clinical symptoms upon accidental contact. Decrease in latex-specific IgE test positivity after 6 years.
Multi-food Allergy	48 patients (Trial) [13]	OIT + Omalizumab vs. OIT + Placebo (16 weeks)	Positive: Lower median per-participant percentage of OIT doses with adverse events in omalizumab group (27%) versus placebo group (68%).
Multi-food Allergy	90 patients (Trial) [14]	OIT + Omalizumab (16 mg/kg or 8 mg/kg) vs. Placebo	Data on specific clinical response rates not explicitly detailed in the source text.
Peanut Allergy	23 patients [16]	Peanut OIT + Omalizumab	Positive: All reached 2,800 mg maintenance dose in median 10 weeks. Moderate/systemic reactions rare on full dose; adverse events increased as omalizumab decreased.

Allergic Bronchopulmonary Aspergillosis (ABPA)

In patients with cystic fibrosis and ABPA who previously failed steroid and antifungal therapies, omalizumab yielded consistently positive results. Improvements were recorded in both pulmonary function (FEV1) and serological markers (total IgE) within 8 weeks of therapy [17]. Data are summarized in Table 4.

Table 4. Pulmonary and Serological Changes in ABPA Patients Treated with Omalizumab

Subject	Baseline FEV1 (% predicted)	8-Week FEV1 (% predicted)	Baseline Total IgE (IU/ml)	8-Week Total IgE (IU/ml)	Clinical Outcome
17-year-old male [17]	40%	93%	1,124	363	Positive: Symptom improvement starting after second injection.
28-year-old male [17]	50%	83%	1,105	301	Positive: Clinical condition improved by week 8.
11-year-old male [17]	40%	68%	1,056	456	Positive: Significant clinical improvement.

Discussion

The analysis of omalizumab's off-label application over the past decade reveals a promising, albeit complex, therapeutic potential across a spectrum of IgE-mediated and inflammatory disorders. Interpreted through the lens of current allergological knowledge [4,5], the selective binding of omalizumab to free IgE appears to offer significant clinical benefits beyond its standard indications, though efficacy varies considerably depending on the specific pathogenesis and patient phenotype.

In the context of systemic mastocytosis, our findings contrast the strong clinical improvements observed in individual case reports [6,7] with the lack of statistical significance found in the double-blind, placebo-controlled trial by Distler et al. [8]. While omalizumab successfully reduced the frequency of anaphylaxis and lowered tryptase levels in highly symptomatic patients, the occurrence of severe multisystem adverse reactions in isolated cases highlights a critical unpredictability in patient response [7]. This discrepancy suggests that while omalizumab may stabilize mast cells indirectly by reducing IgE receptor cross-linking, it does not alter the underlying neoplastic proliferation of mast cells, making it a supportive rather than curative intervention.

The application of omalizumab in atopic dermatitis (AD) presents a striking dichotomy between pediatric and adult populations. The positive outcomes in children, characterized by reduced SCORAD indices and decreased reliance on systemic corticosteroids [9,10], support the

working hypothesis that neutralizing IgE in early-stage atopic march can profoundly mitigate skin inflammation. However, the treatment's failure in adult patients with extremely elevated IgE levels (often exceeding 40,000–60,000 IU/ml) exposes a fundamental pharmacological limitation [11]. In such hyper-IgE states, standard dosing regimens are likely insufficient to neutralize free IgE adequately, leading to the observed exacerbations. The suggestion by Nečas et al. to utilize immunoadsorption prior to omalizumab initiation presents a logical, mechanism-based workaround to this limitation [11].

Regarding IgE-mediated food and latex allergies, the reviewed literature solidifies omalizumab's role as an invaluable adjunct to oral immunotherapy (OIT). By raising the threshold for allergic reactions, omalizumab facilitates rapid and safer desensitization [13,16]. Similarly, in allergic bronchopulmonary aspergillosis (ABPA) complicating cystic fibrosis, omalizumab proved highly effective as a rescue therapy when standard corticosteroid and antifungal treatments failed, breaking the cycle of severe respiratory exacerbations and lung function decline [17].

In the broadest possible context, these findings underscore a paradigm shift toward precision medicine and the use of biologics for rare or recalcitrant immunologic diseases. However, this study and the current body of literature possess several significant shortcomings. The primary limitation is the heavy reliance on case reports and small case series, which inherently carry a high risk of publication bias — successful off-label uses are far more likely to be published than treatment failures. Furthermore, the retrospective nature of many included studies and the glaring lack of large-scale, randomized, double-blind, placebo-controlled trials for most of these indications severely limit the statistical power and generalizability of the conclusions. The methodologies across the reviewed papers also lack standardized dosing protocols for off-label use, often inappropriately extrapolating dosing nomograms intended for asthma.

Practical Implications

Despite these limitations, the practical implications of this review are substantial for clinical practice. Omalizumab can be considered a viable, life-improving rescue therapy for patients with highly symptomatic indolent systemic mastocytosis and for cystic fibrosis patients suffering from refractory ABPA. For food allergies, it should be recognized as a powerful tool to secure the safety of OIT, provided that clinicians strictly monitor patients during the drug tapering phase due to the high risk of rebound anaphylaxis. In severe atopic dermatitis, omalizumab is a practical option for pediatric patients, but clinicians should avoid it as a monotherapy in adults with massively elevated IgE levels.

Future Research Directions

Future research must prioritize large, multi-center randomized controlled trials to establish disease-specific dosing nomograms that do not solely rely on asthma parameters. Further investigation is critically needed to evaluate the efficacy and safety of combining omalizumab with pre-treatment immunoadsorption in hyper-IgE phenotypes. Finally, long-term observational studies are required to determine the safety profile and the potential for sustained disease remission following the discontinuation of prolonged off-label omalizumab therapy.

Conclusions

The off-label use of omalizumab demonstrates promising but highly variable efficacy across different IgE-mediated and inflammatory disorders, heavily dependent on patient phenotype and the specific pathogenesis of the disease:

Systemic Mastocytosis: Omalizumab can effectively reduce the frequency of anaphylaxis and lower basal tryptase levels in select, highly symptomatic patients. However, overall statistical significance remains mixed in larger trials, and the potential for severe multisystem adverse reactions requires careful patient monitoring.

Atopic Dermatitis: The therapeutic response is highly dichotomous. Omalizumab is a highly effective intervention in pediatric patients, significantly reducing disease severity and the need for systemic steroids. Conversely, it is largely ineffective and potentially counterproductive as a monotherapy in adult patients with massively elevated baseline IgE levels.

IgE-Mediated Food and Latex Allergies: Omalizumab serves as a highly valuable adjunctive therapy to oral immunotherapy (OIT). It significantly lowers the rate of adverse allergic reactions and facilitates rapid, safe up-dosing, though patients remain at risk of adverse events if the omalizumab dosage is tapered too quickly.

Allergic Bronchopulmonary Aspergillosis (ABPA): In patients with cystic fibrosis who have failed standard steroid and antifungal therapies, omalizumab acts as a highly reliable rescue therapy. It consistently yields rapid improvements in pulmonary function (FEV1) and notable reductions in total serum IgE levels.

Finally, while omalizumab presents a powerful biologic tool for recalcitrant immunologic conditions, its successful off-label application requires highly individualized, disease-specific dosing protocols rather than standard asthma nomograms.

Supplementary Materials

Not applicable.

Author's Contribution

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Funding Statement

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Acknowledgements

Not applicable.

Conflict of Interest Statement

The authors declare no conflicts of interest.

Data Availability Statement

The data presented in this study are available upon request from the corresponding author.

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