

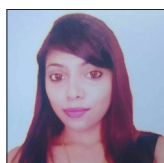


Review Article

Biologics in Asthma: A Paradigm Shift in Treatment for Severe Asthma Patients

Anima Rout¹ , Amrit Prakash² , Elisha Paikray³ , Sangram Keshari Mohapatra⁴ , Ratikanta Tripathy³

¹Department of Pharmacology, Kalinga Institute of Medical Sciences, Kalinga Institute of Industrial Technology Deemed to be University, Bhubaneswar, ²Department of Pharmacology, S.C.B Medical College and Hospital, Cuttack, ³Department of Pharmacology, Kalinga Institute of Medical Sciences, Kalinga Institute of Industrial Technology, ⁴Department of Pulmonary Medicine, Kalinga Institute of Medical Sciences, Kalinga Institute of Industrial Technology Deemed to be University, Bhubaneswar, Odisha, India.



***Corresponding author:**

Elisha Paikray,
Department of Pharmacology,
Kalinga Institute of Medical
Sciences, Kalinga Institute
of Industrial Technology,
Bhubaneswar, Odisha, India.

elisha.paikray@kims.ac.in

Received: 07 July 2025

Accepted: 13 November 2025

Published: 20 January 2026

DOI

10.25259/GJMPBU_43_2025

Quick Response Code:



ABSTRACT

Asthma remains a significant global health concern, with a notable burden in India. Despite advancements in asthma treatment, a subset of patients continues to experience uncontrolled symptoms and frequent exacerbations, leading to increased morbidity, mortality, and healthcare costs. Biologics have emerged as a promising addition to standard therapies, offering targeted, precision treatment for severe asthma patients. This comprehensive review explores the role of biologics in managing severe asthma, focusing on their target site, clinical efficacy, safety profiles, and their future prospects. Various biologics, including anti-immunoglobulin E, anti-interleukin (IL)-5, anti-IL-4/IL-13, and anti-IL-17, have demonstrated efficacy in controlling symptoms and reducing exacerbations in different patients according to their profile. The review also highlights the potential of novel biologics targeting alarmins and emerging predictive biomarkers for personalized medicine in asthma management. The safety profile of biologics appears favorable, with the most common adverse effects being mild injection site reactions. However, careful patient assessment and regular monitoring are essential to identify and manage potential risks. While biologic therapies have shown remarkable effectiveness in managing severe asthma, their accessibility and cost-effectiveness remain challenges in some regions. Overall, biologics represent a paradigm shift in the treatment of severe asthma, offering targeted and personalized therapies that significantly enhance disease control and improve patient outcomes. This review also emphasizes the importance of continued research and development in the field, indicating a promising future for biologics in asthma management.

Keywords: Asthma, Biologics, Interleukins, Targeted therapy

INTRODUCTION

Asthma is a common inflammatory condition of the airways, causing narrowing of the airways. It is portrayed as coughing, dyspnea, shortness of breath, chest tightness, and wheezing.^[1] These respiratory symptoms are temporary and can fluctuate in frequency and severity, accompanied by variable airflow restriction during exhalation. Eventually, in many cases, the airflow limitation may become permanent.^[1] Although commonly viewed as manageable, asthma still presents a major global health burden, affecting over 262 million people and responsible for nearly half a million deaths each year.^[1]

In India, the challenge is even more pronounced. According to the Global Burden of Disease Report, 1990–2019, India has an estimated 34.3 million asthma patients, accounting for 13.09% of the global asthma burden. The Indian INSEARCH study revealed an overall adult prevalence

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2026 Published by Scientific Scholar on behalf of Global Journal of Medical, Pharmaceutical, and Biomedical Update

of 2.05%, affecting over 17.23 million adults.^[2] However, the actual burden is likely much higher due to underreporting, regional disparities, and limited access to diagnosis and treatment.^[3]

Despite the shocking numbers, nearly 65% of asthma cases in India remain poorly controlled, leading to frequent exacerbations, emergency hospital visits, lost schooltime and workdays, and diminished quality of life.^[1]

Tragically, India's asthma mortality rate is 3 times the global average, a sobering statistic for a disease that is largely preventable and manageable with proper care. Asthma now accounts for 1 in every 250 deaths globally, with over 80% of those occurring in low- and middle-income countries like India, due to systemic issues such as underdiagnosis, lack of awareness, poor access to inhaler therapy, and growing environmental risks.^[1]

Demographically, asthma impacts a wide area, impacting both children and adults, but severe forms are more prevalent in individuals with certain phenotypes, such as those with allergic asthma or eosinophilic inflammation.

Urban populations are particularly exposed to air pollution, industrial smog, dust mites and indoor smoke, and sedentary lifestyles significantly worsen symptoms making them more vulnerable. Notably, even moderate Air Quality Index levels (51–100) can aggravate asthma, while levels over 100 pose serious risks, especially to children and the elderly.^[4]

The diagnosis of asthma is mostly made on the history of characteristic symptom patterns and depends on expiratory airflow limitation. Clinicians do not solely rely on symptoms, and consider additional objective lung function tests – such as spirometry, measuring reversibility after bronchodilator administration (e.g., changes in forced expiratory volume in 1 s [FEV₁] and FEV₁/Forced vital capacity [FVC]) and tracking daily fluctuations in peak expiratory flow – to support or rule out an asthma diagnosis. Often, multiple tests are required to definitively establish asthma or to rule out other potential causes of respiratory symptoms. These measures provide valuable insights beyond symptoms alone.^[1]

Case study: Rohan, a 12-year-old boy from Delhi's urban slums

Rohan, a cheerful and active boy, was first diagnosed with severe persistent asthma at just 8 years of age. Living in one of Delhi's densely populated slums, he is constantly exposed to toxic levels of air pollution (with PM_{2.5} levels often exceeding 150 µg/m³), household smoke from open-fire cooking, and seasonal allergens. Although he uses a basic inhaler, his condition remains poorly controlled due to inconsistent access to preventive treatment and limited healthcare awareness in his community. Over the past year, Rohan has endured repeated emergency hospital visits,

often struggling to breathe during the night, missing weeks of school, and being unable to play or study like his peers. His condition was underdiagnosed for several years, leading to progressive breathlessness, and he has required multiple intensive care unit admissions.

His story is just one of millions — a clear reflection of the urgent need for structured asthma care, early diagnosis, routine follow-up, and most critically, public health policies that address air quality, access to inhalers, and community awareness.

Current status and challenges

Global Initiative for Asthma (GINA) is a tool which provides evidence-based guidelines for asthma management. The Standard Controller Therapy (steps 3–5) recommended for asthma patients involves low-dose inhaled corticosteroid (ICS), Short-Acting Beta-Agonist (SABA), and Long-Acting Beta-Agonist (LABA) for maintenance and reliever therapy (MART).^[2]

Before considering any step up, the diagnosis is to be confirmed, and common problems evaluated or assessed in adults (Steps 1–2 combined) who were considered by a clinician to have mild asthma, were taking SABA alone, or had controlled asthma on daily low-dose ICS or leukotriene receptor antagonist.^[3] The preferred step 3 treatment is the regimen with low-dose ICS-formoterol as MART. If needed, the maintenance dose of ICS-formoterol can be increased with the number of maintenance inhalations.^[3]

Even though asthma treatments have improved significantly, some patients continue to experience uncontrolled symptoms, frequent exacerbations, and increased hospitalizations.^[4] Recently, there has been an increase in morbidity and mortality, an increase in healthcare expenditure, and a decrease in quality of life as a result of the disease.^[4] For patients with severe asthma, high-dose inhaled or oral steroids are given along with LABA. Drugs such as tiotropium, leukotriene modifiers, and biologics are also considered in addition to MART therapy. Biologics are recommended in the step 5 category for the management of moderate-to-severe asthma.^[5]

They have emerged as an essential element in the management of severe asthma, offering targeted therapies that promise significant improvement in patients with uncontrolled disease. These therapies, which include monoclonal antibodies that block specific molecules involved in the inflammatory processes of asthma, are particularly beneficial for individuals with eosinophilic or allergic asthma who fail to achieve adequate control with standard therapies such as ICSs.

The demand for biologics has increased as the global burden of severe asthma rises, with conventional treatments

frequently proving ineffective in controlling symptoms. However, challenges remain in their widespread use. The high cost of biologic therapies is a significant barrier, limiting access for many patients, especially in low- and middle-income countries. In addition, biologics require administration via injection or infusion, which can be inconvenient and may deter patient adherence. There is also a need for further research to better understand which patients will benefit most from biologic therapies and to improve long-term safety.

This comprehensive review article seeks to investigate the function of biologics, modes of action, clinical efficacy, safety profiles, their present role and prospective future in the treatment of uncontrolled severe asthma.

BIOLOGICS

Biologics, a class of advanced therapies that specifically target the underlying mechanisms of asthma, have emerged as a promising solution for patients with severe asthma, especially those with allergic or eosinophilic phenotypes. They are preferred as an add-on therapy with ICS-LABA for patients having symptoms despite standard maintenance therapy.^[2] They also have a role in controlling the symptoms and side effects of corticosteroid therapy by following a dose-reduction strategy.

Traditional treatments primarily target the symptoms rather than the underlying causes of asthma, leaving many individuals with uncontrolled inflammation and airway hyperresponsiveness. Biologics, which are advanced, targeted therapies designed to address the specific immunological mechanisms behind asthma, offer a promising solution. By focusing on key inflammatory pathways, such as interleukin (IL)-4, IL-5, and Immunoglobulin E (IgE), biologics can reduce the frequency and severity of exacerbations, improving lung function and decreasing dependence on oral steroids.^[6] As asthma management evolves, biologics are becoming an essential option, particularly for patients with severe asthma [Table 1].

DIAGNOSING ASTHMA- CLINICAL AND FUNCTIONAL INSIGHT

Asthma is a chronic condition characterized by hallmark symptoms of intermittent dyspnea, cough, and wheezing. However, it can be challenging to distinguish asthma from other respiratory illnesses due to the nonspecific nature of these symptoms. The diagnosis of asthma relies on persistent respiratory symptoms and confirmation of expiratory airflow obstruction through spirometry. This essential diagnostic tool assesses lung function and plays a central role in confirming asthma. It particularly measures the ratio of FEV₁/FVC, i.e., FEV₁ related to FVC. Airflow obstruction

is typically indicated when the FEV₁/FVC ratio falls below the lower limit of normal, often approximated as <70% in adults.^[7] Sometimes, clinicians assess bronchodilator reversibility. A positive response is defined by an increase in FEV₁ of at least 12% and 200 mL, according to the traditional American Thoracic Society (ATS)/European Respiratory Society (ERS) (1991) criteria.^[8] The more recent ERS/ATS (2022) update suggests a positive bronchodilator response if there is an increase of more than 10% of the predicted FEV₁ value.^[9] A reduced FEV₁/FVC ratio, which improves significantly after bronchodilator administration, is a hallmark of reversible airway obstruction characteristic of asthma.^[10] This objective confirmation, paired with a clinical history of symptom triggers and variability, helps differentiate asthma from other respiratory conditions, such as chronic obstructive pulmonary disease.

Management focuses on controlling symptoms and preventing future exacerbations through early detection and personalized, stepwise treatment.

MECHANISMS OF ACTION

Induction of asthma involves a complex interplay of immune system responses, inflammation, and airway remodeling. It is triggered by environmental factors such as allergens, environmental stimulants such as pollens, dust, mites, mold, occupational irritants, or respiratory infections, leading to a cascade of mechanisms [Table 2].

Sensitization and Immune Activation

Allergens such as pollen and dust mites are processed by antigen-presenting cells (APCs), including dendritic or lymphoid cells, in allergic asthma. These APCs present the antigens to T-helper (Th0) cells which then differentiate into Th2 cells. The Th2 cells release cytokines such as IL-4,

Table 1: Biologics - target and current status.

Biologics	Target	Stage	Status
Omalizumab	Ig E	2003	Approved
Mepolizumab	IL-5	2015	Approved
Reslizumab	IL-5	2016	Approved
Benralizumab	IL-5R	2017	Approved
Dupilumab	IL-4a/IL-13	2018	Approved
Tezepelumab	TSLP	2018	Approved
Pitrakinra	IL-4a/IL-13	II	-
Lebrikizumab	IL-13	III	-
Tralokinumab	IL-13	III	-

IL: Interleukin, Ig E: Immunoglobulin E, TSLP: Thymic stromal lymphopoietin

IL-5, and IL-13, triggering a series of actions that attract eosinophils to the airways and activate B cells to produce IgE. This cascade contributes to airway inflammation, remodeling, fibrosis, and epithelial hyperplasia.^[4,11]

IgE and mast cell activation

Upon subsequent allergen exposure, B cells are stimulated and produce IgE [Figure 1]. It then attaches to receptors on mast cells, sensitizing, and stimulating their degranulation. The degranulation of mast cells releases mediators such as histamine, prostaglandins, and leukotrienes. Histamine leads to bronchoconstriction, increased vascular permeability, and mucus secretion. Leukotrienes such as LTC₄, LTD₄, and LTE₄ are potent inducers of prolonged bronchoconstriction, causing airway edema. Prostaglandins such as PGD₂ are mostly responsible for bronchospasm and inflammation. Airway smooth muscle contracts in response to inflammatory mediators such as leukotrienes, histamine, and acetylcholine, reducing airway diameter. This constriction significantly contributes to the symptoms of wheezing and breathlessness.^[12]

Airway inflammation

Inflammatory cells (eosinophils, mast cells, T cells) infiltrate the airway wall, releasing cytokines and chemokines that perpetuate inflammation. Eosinophils sometimes release granules such as eosinophilic cationic protein and major basic protein, which cause damage to airway epithelial cells, heightening the sensitivity to triggers. Allergens such as cold air and exercise stimulate the nerves innervating the highly sensitive airways, causing airway hyperresponsiveness

(AHR). This results in exaggerated bronchoconstriction in response to minimal triggers.^[13]

Airway remodeling

Recurrent allergen exposure causes chronic inflammation of the airways, leading to irreversible structural changes. It causes thickening of airways due to subepithelial fibrosis, which is mediated mostly by transforming growth factor-beta. This thickening further causes hypertrophy and hyperplasia of airway smooth muscle, worsens bronchoconstriction, and causes mucus gland hypertrophy, resulting in permanent loss of lung function.^[14] IL-13 causes proliferation of goblet cells in the airway epithelium, producing excessive mucus. These mucus plugs thicken and obstruct the airways, exacerbating airflow limitation.

TYPES OF ASTHMA

Asthma has been categorized into many types depending on various mechanisms and triggers. Asthma driven by immune response to allergens such as pollen, dust mites, and IgE-mediated pathways is defined as allergic asthma. On the other hand, non-allergic asthma is triggered by non-immune factors such as stress, infections, or cold air. Exercise-induced asthma occurs due to airway constriction during or after physical activity, often caused by rapid breathing of dry air. Occupational asthma arises from exposure to irritants like chemicals or fumes in the workplace. These stimulants act as a triggering factor for the release of mediators such as histamines, leukotrienes, and cytokines, which play a key role in the pathogenesis of asthma, causing bronchoconstriction, and mucus production.^[13]

Biologics	Indication	Clinical benefits
Omalizumab (Xolair)	For moderate-to-severe persistent asthma which are poorly controlled with inhaled corticosteroids	<ul style="list-style-type: none"> • Reduced exacerbations and hospitalizations • Decrease dependence on oral corticosteroids • Improved quality of life.
Mepolizumab (Nucala)	Severe eosinophilic asthma	<ul style="list-style-type: none"> • Significant reduction in asthma exacerbations • Improved lung function • Decreased need for maintenance oral corticosteroids.
Reslizumab (Cinqair)	Severe eosinophilic asthma in adults	<ul style="list-style-type: none"> • Reduced frequency of exacerbations • Improvement in lung function.
Benralizumab (Fasenra)	Severe eosinophilic asthma	<ul style="list-style-type: none"> • Significant decline in asthma exacerbations • Lung function improves • Reduction in usage of oral corticosteroid.
Dupilumab (Dupixent)	Moderate to severe eosinophilic asthma with or without oral corticosteroid-dependent asthma; Atopic dermatitis and Chronic rhinosinusitis with nasal polyps.	<ul style="list-style-type: none"> • Asthma exacerbations reduced • Improvement in lung function • Decrease the need for oral corticosteroid.
Tezepelumab (Tezspire)	Severe asthma, regardless of eosinophil status	<ul style="list-style-type: none"> • Marked reduction in asthma exacerbations • Enhanced lung function • Broad efficacy across various asthma phenotypes.

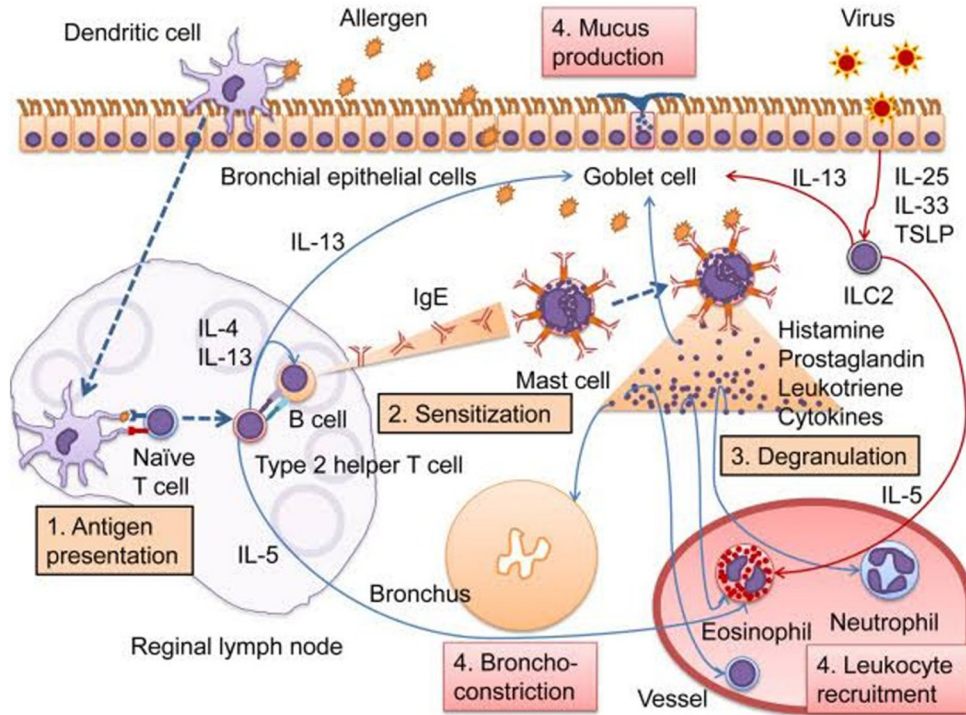


Figure 1: IgE-mediated allergic pathway in asthma.

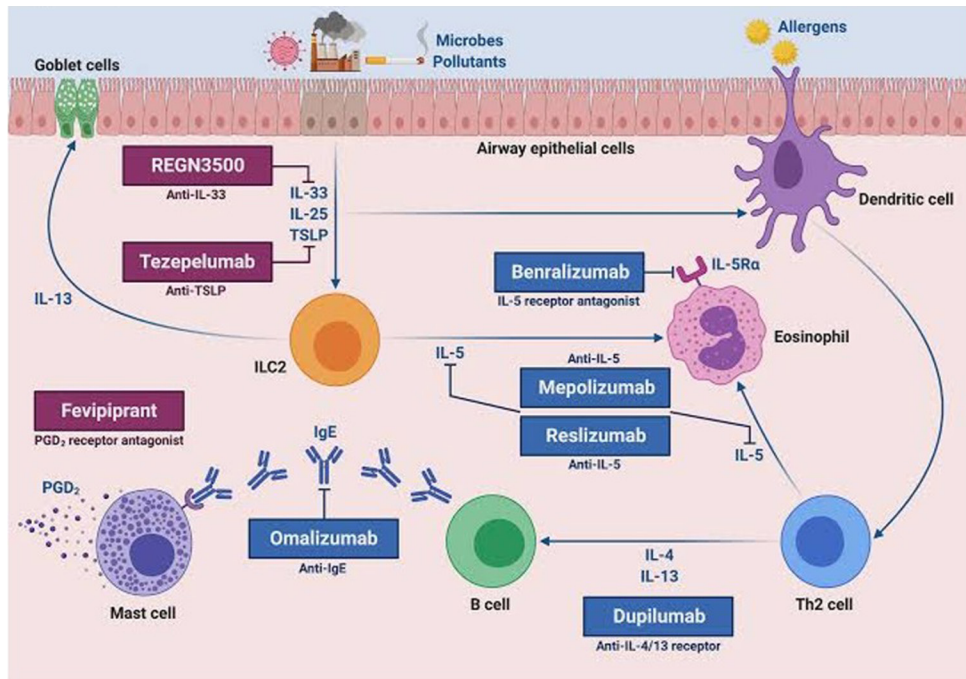


Figure 2: Key inflammatory pathways in Type-2 asthma and biologic targets.

Special variants of asthma

Inflammatory mediators are associated with cough-variant asthma, which increases the sensitivity of both C and Aδ fibers by lowering their activation thresholds. It allows

these nerves to generate action potentials in response to mild chemical, thermal, or mechanical stimuli that would normally be insufficient to trigger activation of these afferent nerves.

Table 3: Clinical efficacy			
Biologics	Patients sample size	Change in annual exacerbation rate	Food and drug administration
Mepolizumab	n=576 (6–11 years)	↓53%	SC 100 mg q4w (56) 40 mg children (27)
Reslizumab	n=953	↓50%	Iv infusion 3 mg/kg q4w
Benralizumab	n=1205 and n=1306	↓45% q4w 51% q8w	Sc 30 mg q4 wsc for first 3 doses then 30 mg q8w sc
Dupilumab	n=1902	↓48% 200 mg 46% 300 mg	Sc initial dose 400 mg then 200 mg q2w initial dose 600 mg then 300 mg q2w

In patients on long-term aspirin, dysregulated arachidonic acid metabolism by enzyme 5-lipoxygenase and cyclooxygenase leads to the generation of leukotrienes, prostaglandins, and thromboxane, which serve as potent bronchoconstrictors.^[12] These patients can suffer from aspirin-exacerbated respiratory disease.

Steroid-resistant asthma, also known as corticosteroid-refractory asthma, is more commonly observed in patients who have been on long-term corticosteroid therapy. This condition occurs when individuals exhibit a poor or diminished response to glucocorticoids, which are typically used to control inflammation in asthma. The resistance may arise due to alterations in glucocorticoid receptor function, increased expression of pro-inflammatory cytokines, or other molecular changes within the immune system that reduce the effectiveness of corticosteroids.^[15] Asthma endotypes can be further categorized based on clinical and inflammatory profiles into eosinophilic, neutrophilic, mixed eosinophilic and neutrophilic, and non-inflammatory (paucigranulocytic) types.^[5,16] Asthma severity can be classified into four categories: intermittent, mild persistent, moderate persistent, and severe persistent. This classification is based on symptom frequency and FEV₁ levels.^[10] Asthma is categorized as childhood-onset or adult-onset depending on the age at which symptoms begin. Childhood-onset asthma is commonly related to allergic triggers and is frequently associated with a pronounced atopic background. On the other hand, adult-onset asthma is non-allergic and is mostly triggered by occupational exposures or infections.^[17]

These classifications help identify the specific type of asthma, enabling tailored treatments and improving disease

management. Severe asthma is a heterogeneous condition due to different phenotypes according to the presence of Type 2 inflammation, which is divided according to the presence (“Type 2 high”) or absence (“non-Type 2 high”). TH2 inflammation characterizes both early onset allergic and late onset eosinophilic phenotypes mediated by IL-4, IL-13 and IL-5.^[5,18] Corticosteroids account for almost all types of asthma cases. Biologics are primarily used for eosinophilic asthma, which includes both allergic and non-allergic type 2 (T2) asthma. For T2-low, neutrophilic severe asthma, monoclonal antibodies address cellular and molecular pathways involved in inflammation, releasing IL-4,5, 13 and their receptors as well as cytokines such as thymic stromal lymphopoietin (TSLP), IL-33, which are responsible for T2-high asthma [Figure 2].^[5,18]

BIOLOGICS IN ASTHMA

By focusing on specific mediators to reduce airway inflammation and bronchoconstriction, these therapies are referred to as targeted “precision” or “personalized” treatments. Predictive biomarkers help in choosing the specific biologics for a particular type of asthma, allowing for individualized treatment and improved patient outcomes. Currently, biologics, which are used as targeted therapy according to GINA guidelines, are omalizumab, benralizumab, mepolizumab etc.^[2]

Anti-Ig E monoclonal antibodies

Omalizumab binds to free circulating IgE (FcεRI and FcεRII) on two Cε3 or CD23 domains and prevents its interaction with mast cell receptors, thus reducing allergic inflammation.^[5] It inhibits the release of histamine and leukotrienes and decreases the exacerbations of severe asthma.

Some studies, such as the INNOVATE Trial and PROSPERO study, demonstrated that omalizumab significantly reduced asthma exacerbations despite blood eosinophil count and fractional exhaled nitric oxide (FeNo).^[19] Omalizumab also has a definite role in improving lung function after 5–9 years of therapy by increasing FEV₁ in 1 s.^[20–22]

IL-5 monoclonal antibodies

Mepolizumab, reslizumab are anti-IL-5 monoclonal antibodies.

In eosinophilic asthma, IL-5 cytokine has a major role in activation and recruitment. Mepolizumab works by binding to IL-5, preventing it from attaching to receptors on eosinophils or blocking its activity.^[13,23] On the other hand, benralizumab targets the IL-5 alpha receptor on eosinophils and induces apoptosis through antibody-dependent cellular cytotoxicity. Hence, mepolizumab and benralizumab are the

most commonly preferred drugs in eosinophilic asthma with blood eosinophil count >150 cells/ μL).^[24]

Like omalizumab, it also reduces exacerbation rate up to 50–70% in patients and also helps in reducing the maintenance dose of oral corticosteroids by 50% as compared to placebo (DREAM Trial).^[4,6,13,25]

Eger *et al.* and some RCT studies showed that subsequent treatment with anti-IL-5 therapy for years can make patients super-responders.^[26] It can also reduce exacerbation rate up to 70% despite having a lower count of ≥ 500 cells/ μL in 2 RCT studies. The SIROCCO and CALIMA trials have demonstrated more rapid eosinophil depletion with reslizumab than benralizumab in eosinophilic asthma.^[27] The OSMEX and BORA study confirmed the sustained efficacy with long-term safety of continuous mepolizumab and Benralizumab treatment.^[24]

Omalizumab and mepolizumab have shown marked improvement in eosinophilic asthma, but they have a very small role in decreasing AHR as compared to etanercept, which is an anti-tumor necrosis factor antibody. Etanercept also has a significant role in refractory asthma, showing improvement of lung function.^[28]

Anti-IL-4 and IL-13 monoclonal antibodies

IL-4/IL-4 Receptor alpha and IL-13 are involved in TH-2 inflammation and play a crucial role in asthma. IL-13 has similar effects to IL-4 primarily affecting structural cells such as epithelial cells, smooth muscle cells, and fibroblasts. It also reduces airway hyperresponsiveness and limits mucus production.^[13] Dupilumab has shown effectiveness in various phenotypes by blocking IL-4/13 receptors. Pascolizumab is another humanized antibody directed against IL-4 receptor, but failed to show efficacy in symptomatic, corticosteroid-naïve asthma patients.^[29]

The LIBERTY Quest and venture trial showed a 50% reduction in the exacerbations rate in steroid-dependent asthma patients. It also improves lung function in asthma patients.^[6,30]

Anti-IL-17 monoclonal antibodies

Bordalumab inhibits the IL-17 signaling pathway associated with neutrophilic inflammation.^[5]

The choice of biologic therapy should be tailored to the individual patient's asthma phenotype, biomarker profile, and clinical history.

NEW BIOLOGICS IN TRIAL

Newer biologics are being developed targeting alarmins and other cytokines such as TSLP, IL-33, and IL-25, involved in T2 inflammatory asthma.^[31-33] Tezepelumab, anti-TSLP is a

cytokine involved in the initiation and activation of the T2 inflammatory cascade.^[13] It is approved for severe asthma of any type without restriction to specific biomarkers. It is used as first-line treatment for improvements in exacerbation rates, irrespective of baseline eosinophil counts, and for reducing reliance on oral corticosteroids.^[13]

Monoclonal antibodies such as Lebrikizumab (RO5490255), an IL-13 antagonist, Etokimab and REGN3500 all acting on IL-33/ST2 receptor, have shown significant effects in patients with uncontrolled steroid-dependent asthma in a Phase II trial.^[13,32,33] Ligelizumab is an anti-IgE biologic having high efficacy over omalizumab for severe allergic asthma. Etokimab is an investigational therapy targeting IL-33 signaling, offering potential benefits for managing broader asthma phenotypes. Another promising molecule, GDC-0334, inhibits the transient receptor potential cation channel A1,^[13,34,35] a nonselective channel activated by mechanical stress, physical strain, or sudden temperature shifts.^[13,36] In addition, drugs such as Canakinumab (anti-IL-1 β), Risankizumab (anti-IL-23), the IL-1 receptor antagonist Anakinra, and granulocyte-macrophage-colony stimulating factor (GM-CSF) inhibitors are in clinical trials, exploring innovative mechanisms to manage asthma and related inflammatory conditions. These emerging treatments reflect the ongoing expansion of therapeutic options targeting diverse pathways involved in asthma pathophysiology [Table 3].^[34,37]

Novel biological targets

It includes novel cytokines, receptors, and signaling molecules that may offer additional therapeutic options for patients with different asthma phenotypes.

Biosimilars

Biosimilars used in asthma treatment are in active development and gaining attention as cost-effective alternatives to originator biologics. Biosimilars for Xolair (omalizumab), which targets IgE in allergic asthma, have been recently approved by the US Food and Drug Administration.^[38] As patents for original biologics expire, biosimilars will likely become more prevalent, increasing patient access to these transformative treatments. These biosimilars are expected to provide effectiveness in controlling moderate to severe allergic asthma while reducing treatment costs.

The development of asthma biosimilars is part of a broader trend in biologics targeting inflammatory diseases.

Safety profiles

The safety profile of biologics in asthma is generally favorable, but like all medications, they are not without potential risks. However, patients should be monitored closely for any signs

of susceptible reactions, infections, or other potential side effects while on biologic treatment. They should also be educated and sensitized about the adverse events and how to seek immediate medical attention if such a reaction occurs.

Biologics are designed to be more targeted by acting on distinct inflammatory pathways that contribute to the progression of asthma, and are potentially safer than conventional systemic therapies such as oral corticosteroids. However, consideration should be given to the potential adverse effects associated with each biologic class.

Mostly, mild-to-moderate injection site reactions (e.g., redness, itching, and swelling) are found with biologics. Although anaphylaxis can occur with patients receiving omalizumab, it is rare. Parasitosis and giardiasis are also associated with omalizumab.^[36,39] Dupilumab and brodalumab are most commonly responsible for adverse drug reactions such as nasopharyngitis (common cold) and headaches in patients.^[40] Some cases of inflammatory bowel disease have also been reported with brodalumab use. Healthcare providers must thoroughly evaluate a patient's medical history, including comorbidities, potential drug interactions, before initiating biologic therapy. Patients should also maintain open communication with their healthcare providers, sharing any side effects or concerns that arise during treatment. By carefully considering patient characteristics and potential risks, healthcare providers can make informed decisions to ensure the safety and efficacy of biologic treatments for asthma. In addition, regular monitoring of patients on biologics is crucial to identify any potential adverse effects early on.

Predictive biomarkers and personalized medicine

It has emerged as a key component of asthma management, particularly in the context of biologic therapies.

Predictive biomarkers

Predictive biomarkers are measurable indicators that provide information about a patient's response to a specific treatment.

Blood eosinophil count

It is increased with response to antibodies, such as mepolizumab, reslizumab, and benralizumab.^[13]

FeNO

It is a key predictive marker specifically for dupilumab targeting eosinophilic asthma.^[16,19]

Periostin is a protein involved in airway remodeling and is associated with type 2 inflammation. High periostin levels can also predict responsiveness to dupilumab and omalizumab.^[17]

Advantages

The integration of predictive biomarkers and personalized medicine in asthma management offers several other advantages. It enables the selection of therapies according to patient profile, increases the likelihood of a positive treatment response, helps in cost reduction, and reduces the risk of unnecessary drug exposure.

Accessibility

Tailored therapies

For patients with uncontrolled asthma despite biologic therapy, the identification of additional treatment options or tailored therapeutic approaches based on individual characteristics, personalized medicine can result in better asthma control, fewer exacerbations, and improved quality of life for patients.

Cost-effectiveness and accessibility of biologics in asthma are crucial considerations when evaluating their impact on healthcare systems and patient populations. Biologics, while highly effective in managing severe asthma, are generally associated with higher costs compared to traditional asthma medications. The initial cost of biologic therapies can be high, including drug acquisition costs and administration expenses. However, evidence suggests that biologics may lead to long-term cost savings due to their ability to reduce asthma exacerbations, hospitalizations, emergency room visits, and systemic steroid use.

Despite the benefits of biologic therapies, accessibility remains a challenge in some regions due to the high cost of biologics. Affordability issues may prevent some patients from accessing these therapies. The availability of insurance coverage for biologic therapies varies across different countries and healthcare plans. Access to biologics may be restricted by insurance companies or national healthcare policies.

Other guidelines and recommendations of biologics

Other guidelines, such as those from ATS and ERS, state that mepolizumab, reslizumab, or benralizumab should be considered for patients with severe eosinophilic asthma who have elevated blood eosinophil levels (≥ 150 cells/ μL) on at least two occasions within a year. The National Institute for Health and Care Excellence guidelines in the United Kingdom and the Canadian Thoracic Society recommend these drugs when blood eosinophils are ≥ 300 cells/ μL on continuous oral corticosteroids.^[41-43]

The future of biologics in asthma management holds significant promise, with ongoing research and developments aimed at further improving patient outcomes and expanding

treatment options. Some biologics initially approved for specific asthma phenotypes are showing efficacy in other asthma subtypes or related respiratory conditions.

CONCLUSION

Biologics have transformed the treatment landscape for severe asthma patients, offering targeted and personalized therapies that significantly improve disease control and patient outcomes. As research continues to advance, biologic therapies are expected to play an increasingly important role in asthma management, providing hope for patients with previously uncontrolled symptoms and paving the way towards more effective and tailored asthma treatments.

Ethical approval: Institutional review board approval is not required.

Declaration of patient consent: Patient's consent not required as there are no patients in this study.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

- Mikkelsen B. The Global Asthma Report 2022. *Int J Tuberc Lung Dis* 2022;26:1-104.
- Global Initiative for Asthma (GINA). 2022 GINA Main Report. Available from: <https://ginasthma.org/gina-reports> [Last accessed on 2023 Aug 31].
- Asthma Global Report. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/pmc8326998> [Last accessed on 2025 May 06].
- McGregor MC, Krings JG, Nair P, Castro M. Role of Biologics in Asthma. *Am J Respir Crit Care Med* 2019;199:433-45.
- Pelaia C, Pelaia G, Crimi C, Longhini F, Lombardo N, Savino R, *et al.* Biologics in Severe Asthma. *Minerva Med* 2022;113:51-62.
- Holguin F, Cardet JC, Chung KF, Diver S, Ferreira DS, Fitzpatrick A, *et al.* Management of Severe Asthma: A European Respiratory Society/American Thoracic Society Guideline. *Eur Respir J* 2020;55:1900588.
- Ponce MC, Sankari A, Sharma S. Pulmonary function tests. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2023. Available from: <https://www.ncbi.nlm.nih.gov/books/nbk482339> [Last accessed on 2025 Aug 28].
- American Academy of Allergy, Asthma and Immunology. Asthma Diagnosis FEV1/FVC. Available from: <https://www.aaaai.org/allergist-resources/ask-the-expert/answers/old-ask-the-experts/fev1-fvc> [Last accessed on 2025 Aug 28].
- Betancor D, Villalobos-Vilda C, Olaguibel JM, Rodrigo-Muñoz JM, Puebla MJ, Arismendi E, *et al.* The New ERS/ATS 2022 Bronchodilator Response Recommendation: Comparison with the Previous Version in an Asthma Cohort. *Arch Bronconeumol* 2023;59:608-11.
- Miranda C, Busacker A, Balzar S, Trudeau J, Wenzel SE. Distinguishing Severe Asthma Phenotypes: Role of Age at Onset and Eosinophilic Inflammation. *J Allergy Clin Immunol* 2004;113:101-8.
- Zhu Z, Homer RJ, Wang Z, Chen Q, Geba GP, Wang J, *et al.* Pulmonary Expression of Interleukin-13 Causes Inflammation, Mucus Hypersecretion, Subepithelial Fibrosis, Physiologic Abnormalities, and Eotaxin Production. *J Clin Invest* 1999;103:779-88.
- Kuruville ME, Lee FE, Lee GB. Understanding Asthma Phenotypes, Endotypes, and Mechanisms of Disease. *Clin Rev Allergy Immunol* 2019;56:219-33.
- Chiu CJ, Huang MT. Asthma in the Precision Medicine Era: Biologics and Probiotics. *Int J Mol Sci* 2021;22:4528.
- Stewart AG, Tomlinson PR, Fernandes DJ, Wilson JW, Harris T. Tumor Necrosis Factor Alpha Modulates Mitogenic Responses of Human Cultured Airway Smooth Muscle. *Am J Respir Cell Mol Biol* 1995;12:110-9.
- Trevor JL, Deshane JS. Refractory Asthma: Mechanisms, Targets, and Therapy. *Allergy* 2014;69:817-27.
- Taunk ST, Cardet JC, Ledford DK. Clinical Implications of Asthma Endotypes and Phenotypes. *Allergy Asthma Proc* 2022;43:375-82.
- Ilmarinen P, Tuomisto LE, Kankaanranta H. Phenotypes, Risk Factors, and Mechanisms of Adult-Onset Asthma. *Mediators Inflamm* 2015;2015:514868.
- Watchorn D, Holguin F. The Use of Biologics in Personalized Asthma Care. *Expert Rev Clin Immunol* 2021;17:1301-9.
- Casale TB, Luskin AT, Busse W, Zeiger RS, Trzaskoma B, Yang M, *et al.* Omalizumab Effectiveness by Biomarker Status in Patients with Asthma: Evidence from PROSPERO, a Prospective Real-World Study. *J Allergy Clin Immunol Pract* 2018;7:156-64.e1.
- Pelaia C, Calabrese C, Barbuto S, Busceti MT, Preianò M, Gallelli L, *et al.* Omalizumab Lowers Asthma Exacerbations, Oral Corticosteroid Intake and Blood Eosinophils: Results of a 5-YEAR Single-Centre Observational Study. *Pulm Pharmacol Ther* 2019;54:25-30.
- Menzella F, Galeone C, Formisano D, Castagnetti C, Ruggiero P, Simonazzi A, *et al.* Real-Life Efficacy of Omalizumab after 9 Years of Follow-Up. *Allergy Asthma Immunol Res* 2017;9:368-72.
- Pace E, Ferraro M, Bruno A, Chiappara G, Bousquet J, Gjomarkaj M. Clinical Benefits of 7 Years of Treatment with Omalizumab in Severe Uncontrolled Asthmatics. *J Asthma* 2011;48:387-92.
- Paoletti G, Pepys J, Casini M, Di Bona D, Heffler E, Goh CY, *et al.* Biologics in Severe Asthma: The Role of Real-World Evidence from Registries. *Eur Respir Rev* 2022;31:210278.
- Gyawali B, Georas SN, Khurana S. Biologics in Severe Asthma: A State-of-the-Art Review. *Eur Respir Rev* 2024;34:240088.
- Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, *et al.* Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma. *N Engl J Med* 2014;371:1189-97.
- Eger K, Kroes JA, Ten Brinke A, Bel EH. Long-Term Therapy Response to Anti-IL-5 Biologics in Severe Asthma-A Real-Life Evaluation. *J Allergy Clin Immunol Pract* 2021;9:1194-200.

27. Casale TB, Pacou M, Mesana L, Farge G, Sun SX, Castro M. Reslizumab Compared with Benralizumab in Patients with Eosinophilic Asthma: A Systematic Literature Review and Network Meta-Analysis. *J Allergy Clin Immunol Pract* 2019;7:122-30.e1.
28. Berry MA, Hargadon B, Shelley M, Parker D, Shaw DE, Green RH, *et al.* Evidence of a Role of Tumor Necrosis Factor Alpha in Refractory Asthma. *N Engl J Med* 2006;354:697-708.
29. Darveaux J, Busse WW. Biologics in Asthma-The Next Step towards Personalized Treatment. *J Allergy Clin Immunol Pract* 2015;3:152-60.
30. Wenzel S, Castro M, Corren J, Maspero J, Wang L, Zhang B, *et al.* Dupilumab Efficacy and Safety in Adults with Uncontrolled Persistent Asthma Despite Use of Medium-to-High-Dose Inhaled Corticosteroids Plus a Long-Acting β_2 Agonist: A Randomised Double-Blind Placebo-Controlled Pivotal Phase 2b Dose-Ranging Trial. *Lancet* 2016;388:31-44.
31. Lambrecht BN, Hammad H. The Airway Epithelium in Asthma. *Nat Med* 2012;18:684-92.
32. Murakami-Satsutani N, Ito T, Nakanishi T, Inagaki N, Tanaka A, Vien PT, *et al.* IL-33 Promotes the Induction and Maintenance of Th2 Immune Responses by Enhancing the Function of OX40 Ligand. *Allergol Int* 2014;63:443-55.
33. Porsbjerg CM, Sverrild A, Lloyd CM, Menzies-Gow AN, Bel EH. Anti-Alarmins in Asthma: Targeting the Airway Epithelium with Next-Generation Biologics. *Eur Respir J* 2020;56:2000260.
34. Nair P, Prabhavalkar KS. Neutrophilic Asthma and Potentially Related Target Therapies. *Curr Drug Targets* 2020; 21:374-88.
35. Gupta A, Ikeda M, Geng B, Azmi J, Price RG, Bradford ES, *et al.* Long-Term Safety and Pharmacodynamics of Mepolizumab in Children with Severe Asthma with an Eosinophilic Phenotype. *J Allergy Clin Immunol* 2019;144:1336-42.e7.
36. Braddock M, Hanania NA, Sharafkhaneh A, Colice G, Carlsson M. Potential Risks Related to Modulating Interleukin-13 and Interleukin-4 Signalling: A Systematic Review. *Drug Saf* 2018;41:489-509.
37. Kalchiem-Dekel O, Yao X, Levine SJ. Meeting the Challenge of Identifying New Treatments for Type 2-Low Neutrophilic Asthma. *Chest* 2020;157:26-33.
38. Tam AC, Badesha J, Guh DP, Bansback N, Peter KK, Hollis A, *et al.* Biosimilar Policies and their Impact on Market Penetration of Adalimumab, Etanercept and Infliximab: A Policy Synthesis and Descriptive Analysis in 13 OECD Countries. *BioDrugs* 2025;39:461-76.
39. Yalcin AD, Bisgin A, Cetinkaya R, Yildirim M, Gorczynski RM. Clinical Course and Side Effects of Anti-IgE Monoclonal Antibody in Patients with Severe Persistent Asthma. *Clin Lab* 2013;59:71-7.
40. Castro M, Mathur S, Hargreave F, Boulet LP, Xie F, Young J, *et al.* Reslizumab for Poorly Controlled, Eosinophilic Asthma: A Randomized, Placebo-Controlled Study. *Am J Respir Crit Care Med* 2011;184:1125-32.
41. National Institute for Health and Care Excellence (NICE). Benralizumab for Treating Severe Eosinophilic Asthma; 2019. Available from: <https://www.nice.org.uk/guidance/ta565> [Last accessed on 2023 Sep 01].
42. National Institute for Health and Care Excellence (NICE). Reslizumab for Treating Severe Eosinophilic Asthma. Available from: <https://www.nice.org.uk/guidance/ta479> [Last accessed on 2025 Jun 31].
43. National Institute for Health and Care Excellence (NICE). Mepolizumab for Treating Severe Eosinophilic Asthma. Available from: <https://www.nice.org.uk/guidance/ta671> [Last accessed on 2025 Jun 31].

How to cite this article: Rout A, Prakash A, Paikray E, Mohapatra SK, Tripathy R. Biologics in Asthma: A Paradigm Shift in Treatment for Severe Asthma Patients. *Glob J Med Pharm Biomed Update*. 2026;21:02. doi: 10.25259/GJMPBU_43_2025