Position statement on the appropriate usage of biologic therapies for asthma in South Africa

R N van Zyl-Smit,[1] MB ChB, FRCP, FCP (SA), MMed (Med), Dip HIV Man (SA), Cert Pulmonology (SA), PhD, ATSF;
M Greenblatt,[2] MB BCh, FCP (SA) FCCP; **C Smith,**[3] MB BCh, FCP (SA), MMed (Int Med), FCCP;
N Singh,[4] MB ChB, FCP (SA), MMed (Int Med), Cert Pulmonology (SA), MPhil (Pulm);
M Wong,[5] MB BCh, FCP (SA), FCCP, FRCP (Lond); **on behalf of the South African Thoracic Society**

[1] *Division of Pulmonology and UCT Lung Institute, Department of Medicine, Faculty of Health Sciences, University of Cape Town and Groote Schuur Hospital, Cape own, South Africa*
[2] *Milpark Hospital, Johannesburg, South Africa*
[3] *Morningside Mediclinic, Johannesburg, South Africa*
[4] *Division of Pulmonology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*
[5] *Division of Pulmonology, Chris Hani Baragwanath Academic Hospital and Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

Corresponding author: *R N van Zyl-Smit (richard.vanzyl-smit@uct.ac.za)*

Executive summary

Biologic therapies such as monoclonal antibodies are highly effective in reducing disease burden (exacerbations/corticosteroid usage/hospitalisation) in patients with severe asthma. These medications are currently prohibitively expensive for widespread use compared with standard inhaled and oral therapy. They are indicated for patients with predominantly type 2-high inflammation.

Judicious use of biologic therapies in the South African context is imperative given the country's limited healthcare resources. The prescription and clinical use of these therapies within the scope of the South African Health Products Regulatory Authority registered indications therefore require clear guidance and appropriate preparatory optimisation to ensure that the appropriate patients receive the correct medication within an acceptable time frame.

Not all patients with difficult-to-treat, or nominally designated as severe, asthma require a biologic therapy in order to be optimally controlled. Simple attention to basic asthma therapeutic principles and treatment of comorbid disease by a clinician with a special interest in asthma may be all that is required.

This position statement, written by senior clinicians from the South African Thoracic Society (SATS), is intended to supplement the SATS asthma treatment recommendation of 2021. It provides clear guidance on the appropriate assessment of patients being considered for biologic therapy and clarifies which background medication is required to initiate a biologic therapy in an evidence-based manner. A alanced consideration of side-effects, scientific evidence and cost is essential to prevent unjustified harm to patients by delaying or denying access to biologic therapy.

A process to endorse biologic therapy has been created in parallel, and forms are available from SATS, along with registration in the severe asthma registry to support clinicians in appropriate assessment and justification for prescription.

Afr J Thorac Crit Care Med 2026;32(1):4376. https://doi.org/10.7196/AJTCCM.2026.v32i1.4376

Severe asthma constitutes a small but clinically significant subset of the asthma population globally and is associated with substantial morbidity and mortality. In South Africa (SA), the recently established South African Thoracic Society (SATS) severe asthma registry will enable more accurate estimations of the local disease burden. International guidelines such as those of the Global Initiative for Asthma (GINA), National Asthma Education and Prevention Program (NAEEP)/National Heart Lung and Blood Insitute (NHLBI) and National Institute for Health and Care Excellence (NICE)/Scottish Intercollegiate Guidelines Network (SIGN) and the Brazilian, Australian and New Zealand guidelines consistently recommend the use of biologic therapies in selected patients with severe asthma, given their proven benefit.[1,2]

The SA asthma guidelines, published in 2021, reference the availability of biologic therapies and provide a broad overview of their suggested usage and indications.[3] This position statement aims to expand upon these brief recommendations by offering specific recommendations/guidance to support clinicians and funders in making informed decisions around providing biologic therapies to patients with severe asthma. GINA has published an extensive document on the assessment and management of difficult-to-treat and severe asthma.[4] It is recommended that clinicians familiarise themselves with this document if they regularly care for patients with difficult-to-treat asthma.

This position statement is not intended to supersede the GINA guideline, but to contextualise the usage of biologic therapies for SA. In this light, the recommendations are based on the original

SOUTH AFRICAN THORACIC SOCIETY

Asthma Biological Therapy Endorsement Form 2026

Name of treating doctor **Practice address**

Name of patient **Age of patient**

Demographics

Height(cm): Gender [◯M/◯F]

Occupation: Self-reported ethnicity: [◯black/◯white/◯mixed/◯Indian/◯other:]

Age of asthma diagnosis(years): Eczema [◯Yes/◯No] Allergic rhinitis [◯Yes/◯No]

Nasal polyposis [◯Yes/◯No] Smoking status [◯current/◯former/◯never] Diabetes [◯Yes/◯No]

Hypertension [◯Yes/◯No] CCF [◯Yes/◯No] Previous TB [◯Yes/◯No]

Obesity [◯Yes/◯No] GORD [◯Yes/◯No] Other:

Asthma severity

In the past 4 weeks, did the patient have: Daytime symptoms more than 2x/ week [◯Yes/◯No]

Any activity limitation [◯Yes/◯No] Any nocturnal symptoms/ awakening [◯Yes/◯No] Reliever use more than 2x/ week [◯Yes/◯No]

(PEF or FEV_1) <80% of predict /personal best: [◯Yes/◯No]

No. of Pred req. exacerbations 12 months. [Number 1-5 and >5]: ◯0 ◯1 ◯2 ◯3 ◯4 ◯5 ◯>5

No. of hospital admission in past 12 months. [Number 1-5 and >5]: ◯0 ◯1 ◯2 ◯3 ◯4 ◯5 ◯>5

No. of episodes of Emergency visits 12 months. [Number 1-5 and >5]: ◯0 ◯1 ◯2 ◯3 ◯4 ◯5 ◯>5

No. of ICU ventilation last 12 months. [Number 1-5 and >5]: ◯0 ◯1 ◯2 ◯3 ◯4 ◯5 ◯>5

No. of ICU vent episodes ever (lifetime). [Number 1-5 and >5]: ◯0 ◯1 ◯2 ◯3 ◯4 ◯5 ◯>5

Medication

		Dose and frequency	Duration at this dose (months)
LABA/ICS (which)			
LAMA (if SIT document here)			
LAMA (which)			
Azithromycin	[◯Yes/◯No]		
Theophylline	[◯Yes/◯No]		
LTRA	[◯Yes/◯No]		
Oral steroids	[◯Yes/◯No]	Oral steroids current duration (months)	
Previous Bronchial Thermoplasty	[◯Yes/◯No]		
Inhaler technique optimised	[◯Yes/◯No]	Adherence optimised [◯Yes/◯No]	Comorbidities optimised [◯Yes/◯No]

Lung function

Pre- bronchodilator FEV_1 (L) Post- bronchodilator FEV_1 (L)

Predicted FEV_1 (L)

FEV_1 pre- bronchodilator (%) FEV_1 post- bronchodilator (%)

Pre-bronchodilator FVC (L) Post- bronchodilator FVC (L)

FEV_1/FVC ratio pre-bronchD FEV_1/FVC ratio post-bronchD (%)

Phenotyping

[ideally within past year – but anytime previously acceptable]

Eosinophil count(absolute) IgE FeNo (PPB)

Skin prick tests done [◯Yes/◯No] Positive for (top 3 only)

Known allergies or other testing [◯Yes/◯No]

Additional comments on management challenges

Biologic of choice

Anti-IgE

- Sensitization on skin prick testing or specific IgE ☐
- Total serum IgE and weight within dosage range ☐
- Exacerbations in last year ☐

Anti-IL-5 / Anti-IL5R

- Exacerbations in last year ☐
- Blood eosinophil> 150 or 300 ☐

Anti-IL4R-alpha (dual blockage of IL-4 & IL-13)

- Exacerbations in last year ☐
- Blood eosinophil ≥150 cells/µl ≤ 1500 cells/µl or Feno > 25ppb ☐
- Taking oral steroid ☐

SATS review committee review

- Confirmed asthma, GINA step 5 ☐
- On maximal inhaler therapy ☐
- Due diligence to inhalers/adherence ☐
- Comorbidities under control ☐
- Fulfils criteria (package insert for specific biologic requested. ☐

The South African Thoracic Society Severe Asthma Group has reviewed this patient request for a Biological Therapy to improve asthma control, reduce risk of long term side effects and exacerbations. This patient is on the documented medications and is within the guidance recommendations of the South African Thoracic Society and Global Initiative for Asthma.

Name:

Date:

Signature:

GINA evidence review, recommendations, and additional detailed literature review with expert consensus, when GRADE (Grading of Recommendations Assessement, Development and Evaluation) or systematic review data were not available. Each statement is contextualised with a strength and evidence evaluation. Clinicians are encouraged to read the GINA severe asthma document to support the management of these patients with severe disease.

Severe asthma

Patients who should be considered for a biologic therapy are those who, despite prescribed appropriate therapy, require a high-dose inhaled corticosteroid (ICS) with a long-acting beta-2-agonist (LABA) and/or oral corticosteroids to achieve control, or remain uncontrolled despite this therapy. The American Thoracic Society (ATS) and European Respiratory Society (ERS) define uncontrolled asthma as fulfilling at least one of the following criteria:

1. Poor symptom control: Asthma Control Questionnaire consistently >1.5, Asthma Control Test <20 (or 'not well controlled' by NAEPP/GINA guidelines).
2. Frequent severe exacerbations: two or more bursts of systemic corticosteroids (>3 days each) during the previous year.
3. Serious exacerbations: at least one hospitalisation, intensive care unit (ICU) stay or mechanical ventilation during the previous year.
4. Persistent airflow limitation: after appropriate bronchodilator withhold, forced expiratory volume in 1 second (FEV_1) <80% predicted (in the face of reduced FEV_1/forced vital capacity (FVC) defined as less than the lower limit of normal).[5]

A clear distinction between the uncontrolled and difficult-to-control asthmatic is needed. A confirmed diagnosis, appropriate exclusion and management of comorbid disease, environmental and allergen review, and optimal medication provision and technically correct inhaler usage are imperative. Details on the approach to difficult-to-control asthma are published in both the SATS and GINA guideline documents.[3,4]

Currently (2026) in SA, three biologic therapies are registered, all of which require confirmation of type 2 (T2)-high inflammation. This requires appropriate assessment prior to the initiation of a biologic therapy.

For patients on GINA-defined step 5 therapy who are being considered for a biologic therapy to control their disease, a comprehensive work-up is required. This assessment should confirm the patient's eligibility, ensure appropriateness of current medication, and guide the selection of the most suitable biologic therapy to be prescribed. The SATS biologic therapy endorsement form should be used as a checklist to ensure that all appropriate steps are taken before initiation of a biologic therapy. There is no minimum time required prior to initiation of a biologic in asthma. It is likely that the patient will have a diagnosis of uncontrolled T2-high asthma for at least a year, and the work-up and requisite optimisation of therapies take at least 3 - 4 months to complete. Recent studies suggest that those who have rapidly escalating intensity of disease respond better than those who have been receiving high-intensity treatment for many years before accessing a biologic.[6] Current recommendations are based on exacerbation frequency, defined as 'two or more bursts of oral steroids' in the past year. Neither 'hospitalisation' nor 'severity' of exacerbation are included in this assessment; systemic risk of oral steroids and physiological consequences of asthma exacerbations are the driver to avoid future exacerbations. Although a judgement call on the potential 'financial outlay' to the funder, or 'ICU and ventilation cost' to the patient, is tempting, this must be rational: multiple oral prednisone courses are cheap and 'easy' to prescribe to fulfil these criteria, and similarly, ICU admissions may be expedient (to the system) or simply a result of poor adherence.[7] A clearly defined exacerbation history is important – but is only one of several criteria to access a biologic therapy.

Overview of the assessment of a patient under consideration for a biologic therapy

1. Patient care should be provided/overseen by a pulmonologist or allergologist/physician with specific interest and experience in asthma care.
   a. There are no international guidelines that prescribe who may initiate such therapy.
   b. This recommendation serves to restrict prescription to those who are experienced in managing complex asthma (not limited to pulmonologists) and have access to the full scope of tests required for assessment.

[Strong recommendation – low evidence]

2. A thorough work-up, including phenotyping of T2 status, is required to confirm the indication for and choice of biologic therapy. The following must be documented:
   a. Full blood count with differential including eosinophil count.
   b. Total immunoglobulin E level.
   c. Chest X-ray (in the SA context with high rates of tuberculosis (TB)/post-TB bronchiectasis, etc., this is mandatory).
   d. Fractional exhaled nitric oxide if available.
   e. If there is suspicion of additional pathologies such as eosinophilic pneumonia, eosinophilic granulomatosis with polyangiitis or allergic bronchopulmonary aspergillosis, or the chest X-ray is abnormal, a high-resolution computed tomography scan should be performed.

[Strong recommendation – good evidence]

3. Adherence and inhaler technique need to be reviewed and optimised over several healthcare visits.
   a. Inhaler technique for both pressurised metered-dose inhalers and dry powder inhalers is ubiquitously substandard and requires continual review and optimisation. Good inhaler technique frequently improves asthma control alongside regular follow-up, as seen in the benefits of placebo arms in clinical trials. Switching to alternative devices should be considered if technique remains suboptimal.

[Strong recommendation – good evidence]

4. Patients who are actively smoking should undergo intensive smoking cessation intervention and have stopped smoking before initiating a biologic.
   a. No smokers have been recruited to any of the biologic therapy development trials.
   b. Very few smoking asthmatics have been recruited to inhaled medication trials, with limited evidence of impact available.

c. There are data indicating that previous smokers do benefit, and a smoking history is therefore not an exclusion criterion. Although no time frame is defined, cessation of smoking for ≤3 months is deemed reasonable for consideration of a biologic therapy if indicated.

[Strong recommendation – low evidence]

5. Background medication should include at least a regular maintenance high-dose ICS/LABA combination with at least daily 800 µg budesonide equivalent.
   a. Although the GINA strategy document indicates that a biologic therapy should be used in place of high-dose inhaled steroids, given the cost-risk ratio in the SA context we recommend that patients should be on high-dose ICS prior to initiation of a biologic therapy.

[Strong recommendation – moderate evidence]

6. Background medication should include a long-acting muscarinic antagonist (LAMA), either as part of single-inhaler triple therapy or as a separate inhaler added to high-dose ICS/LABA.
   a. The registration trials of biologic therapies did not require participants to be on a LAMA prior to study entry. The LAMA trials consistently show significant reduction in exacerbations and improvement in symptoms.[8-11] Given the relatively low cost and low side-effect profile of LAMAs, we recommend that patients be prescribed triple therapy, i.e. LAMA-LABA-ICS combination – either as a single inhaler or in combination.

[Strong recommendation – moderate evidence]

7. There is neither evidence nor rationale for patients to be prescribed maintenance oral corticosteroids prior to initiation of a biologic therapy. However, the need for maintenance oral corticosteroids should prompt the clinician to consider introduction of a biologic therapy.
   a. Regular (daily) use of oral corticosteroids should be avoided at all costs and is not justifiable as a requirement for the use of a biologic therapy. Good data exist showing that initiation of a patient on a biologic therapy who is using background oral corticosteroids will result in dose reduction of the oral corticosteroid.[12-15] The deleterious side-effects of systemic corticosteroids are well documented, and the risks far outweigh the costs and risk of biologic therapy.

[Strong recommendation – strong evidence]

8. There is neither evidence nor rationale for all patients to be prescribed background macrolide therapy prior to initiation of a biologic therapy.
   a. Macrolide therapy (e.g. azithromycin 3 times a week) has been shown to be effective in patients with severe asthma (on high-dose ICS/LABA),[16] but was not a requirement, and was frequently an exclusion criterion, for the registration trials for biologic therapies. GINA furthermore does not recommend their routine use, but they may be considered in those with T2 low disease[1] or if a T2 biologic therapy is not available. There are data showing that macrolide therapy may be of value in patients who experience exacerbations despite use of a biologic therapy.
   b. Long-term macrolide therapy has significant gastrointestinal tract side-effects, and can cause liver dysfunction, hearing loss, visual impairment, QT prolongation and potential macrolide resistance in mycobacterial and non-tuberculous mycobacterial infections.

[Strong recommendation – strong evidence]

Severe asthma checklist. This checklist (supplementary file available online here) is based on the above recommendations. It serves as a guide to the information needed to make a decision on initiating a biologic therapy, and is utilised as part of the SATS endorsement process.

Data availability. Not applicable.

Declaration. RNvZS and MW are members of the editorial board.

Acknowledgements. None.

Author contributions. All authors were involved in the data review, decision-making and evidence grading to compile this manuscript.

Funding. None.

Conflicts of interest. All authors have participated in industry-funded meetings, but no industry input or funding was provided for this statement.

1. Global Initiative for Asthma. 2025 Global Strategy for Asthma Management and Prevention. https://ginasthma.org/wp-content/uploads/2025/11/GINA-2025-Update-25_11_08-WMS.pdf (accessed 20 August 2025).
2. Cloutier MM, Baptist AP, Blake KV, et al. 2020 focused updates to the asthma management guidelines: A report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. J Allergy Clin Immunol 2020;146(6):1217-1270. https://doi.org/10.1016/j.jaci.2020.10.003
3. Lalloo UG, Kalla IS, Abdool-Gaffar S, et al. Guidelines for the management of asthma in adults and adolescents: Position statement of the South African Thoracic Society – 2021 update. Afr J Thorac Crit Care Med 2021;27(4):10.7196/AJTCCM.2021.v27i4.189. https://doi.org/10.7196/AJTCCM.2021.v27i4.189
4. Global Initiative for Asthma. Difficult-to-treat & severe asthma in adolescent and adult patients, v6.0 July 2025. https://ginasthma.org/2025-gina-severe-asthma-guide/ (accessed 20 August 2025).
5. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J 2014;43(2):343-373. https://doi.org/10.1183/09031936.00202013
6. Soendergaard MB, Hjortdahl F, Hansen S, et al. Pre-biologic disease trajectories are associated with morbidity burden and biologic treatment response in severe asthma. Eur Respir J 2025;65(4):2401497. https://doi.org/10.1183/13993003.01497-2024
7. Manyeruke F, Calligaro GL, Raine R, van Zyl-Smit RN. Asthma in the intensive care unit: A review of patient characteristics and outcomes. Afr J Thorac Crit Care Med 2023;29(2):10.7196/AJTCCM.2023.v29i2.212. https://doi.org/10.7196/AJTCCM.2023.v29i2.212
8. Kim LHY, Saleh C, Whalen-Browne A, O'Byrne PM, Chu DK. Triple vs dual inhaler therapy and asthma outcomes in moderate to severe asthma: A systematic review and meta-analysis. JAMA 2021;325(24):2466-2479. https://doi.org/10.1001/jama.2021.7872
9. Kerstjens HAM, Maspero J, Chapman KR, et al. Once-daily, single-inhaler mometasone-indacaterol-glycopyrronium versus mometasone-indacaterol or twice-daily fluticasone-salmeterol in patients with inadequately controlled asthma (IRIDIUM): A randomised, double-blind, controlled phase 3 study. Lancet Respir Med 2020;8(10):1000-1012. https://doi.org/10.1016/S2213-2600(20)30190-9
10. Van Zyl-Smit RN, Chapman KR, Kerstjens HAM, et al. Mometasone/indacaterol/glycopyrronium (MF/IND/GLY) and MF/IND at different MF strengths versus fluticasone propionate/salmeterol xinafoate (FLU/SAL) and FLU/SAL+ tiotropium in patients with asthma. J Asthma Allergy 2023;16:123-134. https://doi.org/10.2147/JAA.S392975
11. Gessner C, Kornmann O, Maspero J, et al. Fixed-dose combination of indacaterol/glycopyrronium/mometasone furoate once-daily versus salmeterol/fluticasone twice-daily plus tiotropium once-daily in patients with uncontrolled asthma: A randomised, phase IIIb, non-inferiority study (ARGON). Respir Med 2020;170:106021. https://doi.org/10.1016/j.rmed.2020.106021

12. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med 2018;378(26):2475-2485. https://doi.org/10.1056/NEJMoa1804093
13. Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. N Engl J Med 2017;376(25):2448-2458. https://doi.org/10.1056/NEJMoa1703501
14. McDougall C, Hoenck HH, Peter JG. Systemic and non-systemic corticosteroid therapies: Adverse effects of both short burst and cumulative long-term dosing. Curr Allergy Clin Immunol 2025;38(1):12-22.
15. Chen W, Tran TN, Sadatsafavi M, et al. Impact of initiating biologics in patients with severe asthma on long-term oral corticosteroids or frequent rescue steroids (GLITTER): Data from the International Severe Asthma Registry. J Allergy Clin Immunol Pract 2023;11(9):2732-2747. https://doi.org/10.1016/j.jaip.2023.05.044
16. Gibson PG, Yang IA, Upham JW, et al. Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): A randomised, double-blind, placebo-controlled trial. Lancet 2017;390(10095):659-668. https://doi.org/10.1016/S0140-6736(17)31281-3

Received 20 October 2025. Accepted 4 March 2026. Published 31 March 2026.