

# Journal Pre-proof

Global Initiative for Asthma (GINA) Strategy 2021 – Executive summary and rationale for key changes

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## Global Initiative for Asthma (GINA) Strategy 2021 Executive summary and rationale for key changes

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## GINA 2021 Executive summary

## Abstract

The Global Initiative for Asthma (GINA) Strategy Report provides clinicians with an annually updated evidence-based strategy for asthma management and prevention, which can be adapted for local circumstances (e.g., medication availability). This article summarizes key recommendations from GINA 2021, and the evidence underpinning recent changes.

GINA recommends that asthma in adults and adolescents should not be treated solely with short-acting beta<sub>2</sub>-agonist (SABA), because of the risks of SABA-only treatment and SABA overuse and evidence for benefit of inhaled corticosteroid (ICS). Large trials show that as-needed combination ICS-formoterol reduces severe exacerbation by ~60% in mild asthma compared with SABA alone, with similar exacerbation symptom, lung function and inflammatory outcomes as daily ICS plus as-needed SABA.

Key changes in GINA 2021 included division of the treatment figure for adults and adolescents into two tracks. Track 1 (preferred) has low-dose ICS-formoterol as the reliever at all steps: as-needed only in Steps 1-2 (mild asthma) and with daily maintenance ICS-formoterol (maintenance and reliever therapy, MART) in Steps 3-5. Track 2 (alternative) has as-needed SABA across all steps, plus regular ICS (Step 2) or ICS-long-acting beta<sub>2</sub>-agonist (LABA) (Steps 3-5). For adults with moderate to severe asthma, GINA makes additional recommendations in Step 5 for add-on long-acting muscarinic antagonists and azithromycin, with add-on biologic therapies for severe asthma. For children 6-11 years, new treatment options are added at Steps 3-4.

Across all age groups and levels of severity, regular personalized assessment, treatment of modifiable risk factors, self-management education, skills training, appropriate medication adjustment and review remain essential to optimize asthma outcomes.

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## Introduction

Asthma is a serious global health problem affecting all age groups.<sup>1</sup> Its prevalence has increased in many countries, especially among children. The Global Initiative for Asthma (GINA) aims to improve the diagnosis, management, and prevention of asthma by providing an up-to-date evidence-based strategy and tools and practical resources for clinicians worldwide.

GINA was established through a 1993 collaboration between the World Health Organization (WHO) and the US National Heart, Lung, and Blood Institute to develop a strategy for the diagnosis and management of asthma.<sup>2</sup> The Global Strategy for Asthma Management and Prevention (GINA strategy report) has been updated annually since 2002, to provide clinicians with up-to-date evidence-based recommendations as new evidence emerges and new therapies are approved. The GINA strategy reports are under continual review by the Science Committee. GINA methodology<sup>3</sup> involves evaluation of new evidence identified from a twice-yearly rolling review of original research and systematic reviews (not limited to specific PICO [population/intervention/comparison/outcome] questions) assessment of its impact on existing or new recommendations, and consideration of whether and how it should be integrated into the overall asthma management strategy. GINA is independent of industry.

This article summarizes key recommendations from the 2021 GINA strategy report,<sup>4</sup> published in April 2021, and briefly summarizes the evidence and rationale for recent important changes.

## Key recommendations [text box]

1. Diagnosis: In adults, adolescent and children  $\geq 6$  years, confirm the diagnosis of asthma before starting controller treatment whenever possible, as it is often more difficult afterwards.

In children  $< 5$  years, recurrent wheezing is common, but asthma is more likely if they have wheezing or coughing with exercise/laughing/crying in the absence of respiratory infections, and if they have a history of eczema or allergic rhinitis.

2. Personalized assessment and treat-review cycles: Asthma management should be personalized and adjusted in a continual cycle of assessment, treatment and review, to minimize symptoms and prevent exacerbations. Consider symptom control, risk factors for exacerbation and side effects, lung function, comorbidities, self-management skills, and patient and/or caregiver goals, preferences and satisfaction.

3. Comprehensive care: Asthma management is not  $\mu$ R-Size-fits- D O t O n f l u d e s n o t o n l y medication, but also treatment of modifiable risk factors and comorbidities, non-pharmacological strategies and education and skills training, particularly for inhaler technique and adherence.

4. Inhaled corticosteroids (ICS): Asthma in adults and adolescents should not be managed solely with short-acting beta<sub>2</sub>-agonists (SABA). Instead, to reduce the risk of severe exacerbations and to control symptoms, all adults and adolescents with asthma should be treated with ICS-containing therapy: either regularly every day or, in mild asthma, with ICS-formoterol taken as needed for symptom relief. ICS-containing treatments are also recommended for all children 6-11 years with asthma: either regularly or, in mild asthma, by taking ICS whenever SABA is taken. The past distinction between  $\mu$  L Q W H L a n d  $\mu$  W W O H Q W  $\uparrow$  S H U V l a s t n a m e s a r b i t r a r y and does not predict differential response to ICS.

5. Treatment tracks: In 2021, for clarity, GINA treatment for adults and adolescents was divided into two tracks, depending on the inhaled reliever medication. Across the five steps, treatment may be stepped up or down within a track, using the same reliever at each step, or switched between tracks, according to the S D W L e Q M P preferences:

- x Track 1, with low-dose ICS-formoterol as the reliever. This is the overall preferred approach because it reduces the risk of severe exacerbations, compared with using a SABA reliever (with/without maintenance controller), with similar symptom control, similar lung function, and lower oral corticosteroid (OCS) burden. In Steps 1-2, there are additional reasons for preferring as-needed only ICS-formoterol over as-needed SABA (alone or with daily ICS): (i) Patients with  $\mu$  P L A S T M F can have severe exacerbations, (ii) adherence with daily ICS is almost universally poor in patients with mild or infrequent symptoms, leaving them at high risk of severe exacerbations, and (iii) starting treatment with SABA alone trains patients to regard it as their main asthma treatment. As-needed only ICS-formoterol (without maintenance treatment) in Steps 1-2 should be distinguished from Maintenance And Reliever Therapy (MART)\* in Steps 3-5, where patients also take ICS-formoterol as daily maintenance treatment. MART is also an option for children 6-11 years in Steps 3-4. ICS-formoterol should not be used as a reliever for patients taking a combination of formoterol ICS-long-acting beta<sub>2</sub> agonist (LABA), with/without long-acting muscarinic antagonist (LAMA).
- x Track 2, with SABA as the reliever. This is an alternative approach (e.g. if Track 1 is not possible, or is not preferred by a patient with no exacerbations in the last year). However, before considering a regimen with SABA reliever, consider whether the patient is likely to adhere to controller therapy. If not, they will be exposed to the risks of SABA-only treatment. For Step 1, taking ICS whenever SABA is taken is preferable to SABA alone.

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For either track, GINA provides an integrated approach and decision tree for difficult-to-treat and severe asthma, with add-on therapies in Step 5 for severe asthma including biologic therapy guided by inflammatory phenotype.

6. Children <math>\leq 5</math> years: Manage wheezing episodes initially with inhaled SABA. Consider trialing controller therapy (e.g., for 3 months) if the symptom pattern suggests asthma, alternative diagnoses have been excluded, and respiratory symptoms and/or wheezing episodes are frequent or severe.

7. Stepping up: Before stepping up treatment to control symptoms or prevent exacerbations, confirm that the symptoms are due to asthma and identify and address modifiable risk factors including incorrect inhaler technique, poor medication adherence, environmental exposures, and multimorbidity, and provide patient education.

8. Stepping down: Once asthma is well controlled for 2-3 months, consider stepping down gradually to find the minimum effective dose, monitoring the patient frequently. Step up again if needed.

9. Asthma action plans: As part of supported asthma self-management, provide a personalized written asthma action plan for all patients, tailored to their health literacy, so they know how to recognize and respond to worsening asthma.

10. Referral: Refer patients for expert advice if any of the following apply:

- x The diagnosis of asthma cannot confidently be confirmed. For children <math>\leq 5</math> years, strongly consider referral for further diagnostic investigations if there is very early onset of symptoms, failure to respond to treatment, or features suggesting alternative diagnoses (e.g., hypoxemia, finger clubbing, failure to thrive).
- x Occupational asthma is suspected.



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- x The patient has any risk factors for asthma-related death.
- x Symptoms or exacerbations remain uncontrolled despite medium/high dose ICS-LABA.
- x The patient needs urgent healthcare or OCS more than once a year.
- x There is evidence or high risk of treatment side effects.
- x Food allergy is suspected.

\*also called single inhaler maintenance and reliever therapy (SMART)

## Asthma management during the COVID-19 pandemic

Patients with asthma are not at increased risk of acquiring COVID-19, or of severe COVID-19. Advise patients to continue taking their prescribed asthma medicines, including ICS, alone or in combination with a LABA, and biological therapy for severe asthma.

Avoid the use of nebulizers where possible, due to the risk of viral transmission. Within healthcare facilities, follow local infection control procedures and COVID-19 testing recommendations. Spirometry, peak expiratory flow (PEF) measurement or other aerosol generating procedures (e.g., oxygen therapy, sputum induction, ventilation) are needed.

GINA recommends COVID-19 vaccination for people with asthma, with usual precautions including checking for allergy to vaccine ingredients. Anaphylaxis to foods, insect venom or medications is not a contraindication. Consider giving biological therapies on a different day from COVID-19 vaccine.

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