POCKET GUIDE FOR ASTHMA MANAGEMENT AND PREVENTION

(for Adults and Children Older than 5 Years)

A Pocket Guide for Health Professionals

Updated 2022

BASED ON THE GLOBAL STRATEGY FOR ASTHMA MANAGEMENT AND PREVENTION

GLOBAL INITIATIVE FOR ASTHMA

ASTHMA MANAGEMENT AND PREVENTION

for adults and children older than 5 years

A POCKET GUIDE FOR HEALTH PROFESSIONALS

Updated May 2022

GINA Science Committee

Chair: Helen Reddel, MBBS PhD

GINA Board of Directors

Chair: Louis-Philippe Boulet, MD

GINA Dissemination and Implementation Committee

Chair: Mark L. Levy, MD

GINA Program

Rebecca Decker, BS, MSJ

Kristi Rurey, AS

Names of members of the GINA Committees are listed on page 50.

LIST OF ABBREVIATIONS

BDP	Beclometasone dipropionate
COPD	Chronic obstructive pulmonary disease
CXR	Chest X-ray
DPI	Dry powder inhaler
FeNO	Fraction of exhaled nitric oxide
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GERD	Gastroesophageal reflux disease
ICS	Inhaled corticosteroids
ICS-LABA	Combination ICS and LABA
Ig	Immunoglobulin
IL	Interleukin
IV	Intravenous
LABA	Long-acting beta$_2$-agonist
LAMA	Long-acting muscarinic antagonist
LTRA	Leukotriene receptor antagonist
n.a.	Not applicable
NSAID	Nonsteroidal anti-inflammatory drug
O_2	Oxygen
OCS	Oral corticosteroids
PEF	Peak expiratory flow
pMDI	Pressurized metered dose inhaler
SABA	Short-acting beta$_2$-agonist
SC	Subcutaneous
SLIT	Sublingual immunotherapy
TSLP	Thymic stromal lymphopoietin

The reader acknowledges that this **Pocket Guide** is a brief summary of the GINA 2022 report for primary health care providers. It does NOT contain all of the information required for managing asthma, for example, about the safety of treatments, and it should be used in conjunction with the full GINA 2022 report. When assessing and treating patients, health professionals are strongly advised to use their own professional judgment and to take into account local and national regulations and guidelines. GINA cannot be held liable or responsible for inappropriate healthcare associated with the use of this document, including any use which is not in accordance with applicable local or national regulations or guidelines.

TABLE OF CONTENTS

TABLE OF FIGURES

ADVICE ON ASTHMA MANAGEMENT DURING THE COVID-19 PANDEMIC

Overall, people with asthma do not appear to be at increased risk of being infected with COVID-19, or of having severe COVID-19

People with well-controlled asthma do not appear to be at increased risk of severe COVID-19 or COVID-19-related death, but the risk of COVID-19 death is increased in people who recently needed oral corticosteroids (OCS) for their asthma and in hospitalized patients with severe asthma. In a meta-analysis, the risk of COVID-19-related mortality in people with asthma appeared to be *lower* than in people without asthma.

In 2020, many countries saw a decrease in asthma exacerbations and influenza-related illness, possibly due to handwashing, masks and physical distancing that reduced respiratory infections including influenza.

Advise patients with asthma to continue taking their prescribed asthma medications, particularly inhaled corticosteroid (ICS) medications

Asthma medications should be continued as usual during the COVID-19 pandemic. This includes ICS-containing medications (alone or in combination), and add-on therapy including biologic therapy for severe asthma. Stopping ICS often leads to potentially dangerous worsening of asthma. Advise patients to discuss with you before stopping *any* asthma medication. This includes OCS in the small proportion of patients with severe asthma for whom these are needed as last resort.

Make sure that all patients have a written asthma action plan

A written action plan can be handwritten, printed, digital or pictorial. It tells the patient how to recognize worsening asthma, how to increase their reliever and controller medications, and when to seek medical help. A short course of OCS may be needed during severe asthma flare-ups (exacerbations or attacks). See the GINA 2022 report Box 4-2 for more information about the options for asthma action plans.

When COVID-19 is confirmed or suspected, or local risk is moderate or high, avoid using nebulizers where possible due to the risk of transmitting infection to healthcare workers and other patients

Instead, to deliver short-acting beta$_2$-agonist for acute asthma in adults and children, use a pressurized metered-dose inhaler and spacer, with a mouthpiece or tightly fitting face mask, if required.

Avoid spirometry in patients with confirmed/suspected COVID-19

In healthcare facilities, follow local COVID-19 testing recommendations and infection control procedures if spirometry or peak flow measurement is needed. Use of an in-line filter minimizes the risk of transmission during

spirometry, but patients often cough *after* spirometry. Coach the patient to stay on the mouthpiece if they need to cough.

Follow local infection control recommendations if other aerosol-generating procedures are needed

These include oxygen therapy (including with nasal prongs), sputum induction, manual ventilation, non-invasive ventilation and intubation. U.S. Centers for Disease Control and Prevention (CDC) recommendations are found here.

Follow local health advice about hygiene strategies and use of personal protective equipment as new information becomes available in your country or region.

At present, based on the benefits and risks, GINA recommends people with asthma should be up to date with COVID-19 vaccination, including boosters if available

Many COVID-19 vaccines are in use, and allergic reactions are rare. Patients with a history of severe allergic reaction to a COVID-19 vaccine ingredient (e.g. polyethylene glycol for Pfizer/BioNTech or Moderna, or polysorbate 80 for AstraZeneca or J&J/Janssen) should receive a different vaccine type. However, people with anaphylaxis to foods, insect venom, or other medications can safely receive COVID-19 vaccines.

Usual vaccine precautions apply. For example, ask about history of allergy to vaccines or their components, and delay vaccination if the patient has a fever or other infection.

GINA suggests that, if possible, the first dose of a biologic therapy for severe asthma and COVID-19 vaccination should not be given on the same day.

Remind people with asthma to have an influenza vaccination

CDC (advice here) now advises that influenza vaccine and COVID-19 vaccine can be given on the same day.

Additional resources

The CDC website provides up-to-date information about COVID-19 for health professionals here and for patients here.

The website of the World Health Organization (WHO) provides comprehensive advice for health professionals and health systems about prevention and management of COVID-19 here.

Global Initiative for Asthma, July 05, 2022

ABOUT ASTHMA AND GINA

Asthma affects an estimated 300 million individuals worldwide. It is a serious global health problem affecting all age groups, with increasing prevalence in many developing countries, rising treatment costs, and a rising burden for patients and the community. Asthma still imposes an unacceptable burden on health care systems, and on society through loss of productivity in the workplace and, especially for pediatric asthma, disruption to the family. Asthma still contributes to many deaths worldwide, including among young people. Approximately 96% of asthma deaths are in low- and middle-income countries.

Health care providers managing asthma face different issues globally, depending on the local context, the health system, and access to resources.

The Global Initiative for Asthma (GINA) was established to increase awareness about asthma among health professionals, public health authorities and the community, and to improve prevention and management through a coordinated worldwide effort. GINA prepares annually updated scientific reports on asthma, encourages dissemination and implementation of the recommendations, and promotes international collaboration on asthma research.

The Global Strategy for Asthma Management and Prevention provides a comprehensive and integrated approach to asthma management that can be adapted for local conditions and for individual patients. It focuses not only on the existing strong evidence base, but also on practical advice for clinicians. The report is updated each year based on a twice-yearly review of new evidence, both original research and systematic reviews. For GINA methodology, see www.ginasthma.org/aboutus/methodology/.

The GINA 2022 report and other GINA publications listed on page 50 can be obtained from www.ginasthma.org.

WHAT IS KNOWN ABOUT ASTHMA?

Asthma is a common and potentially serious chronic disease that imposes a substantial burden on patients, their families and the community. It causes respiratory symptoms, limitation of activity, and flare-ups (attacks) that sometimes require urgent health care and may be fatal.

Fortunately, asthma can be effectively treated, and most patients can achieve good control of their asthma. Good asthma control means that patients can:

- ✓ Avoid troublesome symptoms during day and night
- ✓ Need little or no reliever medication
- ✓ Have productive, physically active lives
- ✓ Have normal or near normal lung function
- ✓ Avoid serious asthma flare-ups (exacerbations, or attacks)

Asthma affects all levels of society. Olympic athletes, famous leaders and celebrities, and ordinary people live successful and active lives with asthma.

What is asthma? Asthma causes respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough that vary over time including in their frequency and intensity. These symptoms are associated with variable expiratory airflow, i.e. difficulty breathing air out of the lungs due to bronchoconstriction (airway narrowing), airway wall thickening, and increased mucus. Some variation in airflow can also occur in people without asthma, but it is greater in untreated asthma. There are different types of asthma (also called phenotypes), and different underlying disease processes.

Factors that may trigger or worsen asthma symptoms include viral infections, allergens at home or work (e.g. house dust mite, pollens, cockroach), tobacco smoke, exercise and stress. These responses are more likely when asthma is uncontrolled. Asthma can also be induced or symptoms triggered by some drugs, e.g. beta-blockers, and (in some patients), by aspirin or other NSAIDs.

Asthma flare-ups (also called exacerbations or attacks) can be fatal, even in people with apparently mild asthma. They are more common and more severe when asthma is uncontrolled, and in some high-risk patients. All patients should have a written asthma action plan; “written” includes handwritten, printed, digital or pictorial, not just verbal instructions.

ICS-containing treatment markedly reduces the frequency and severity of asthma symptoms and markedly reduces the risk of flare-ups or death.

Asthma treatment should be customized to the individual patient, taking into account their level of symptom control, their risk factors for exacerbations, phenotypic characteristics, and preferences, as well as the effectiveness of available medications, their safety, and their cost to the payer or patient.

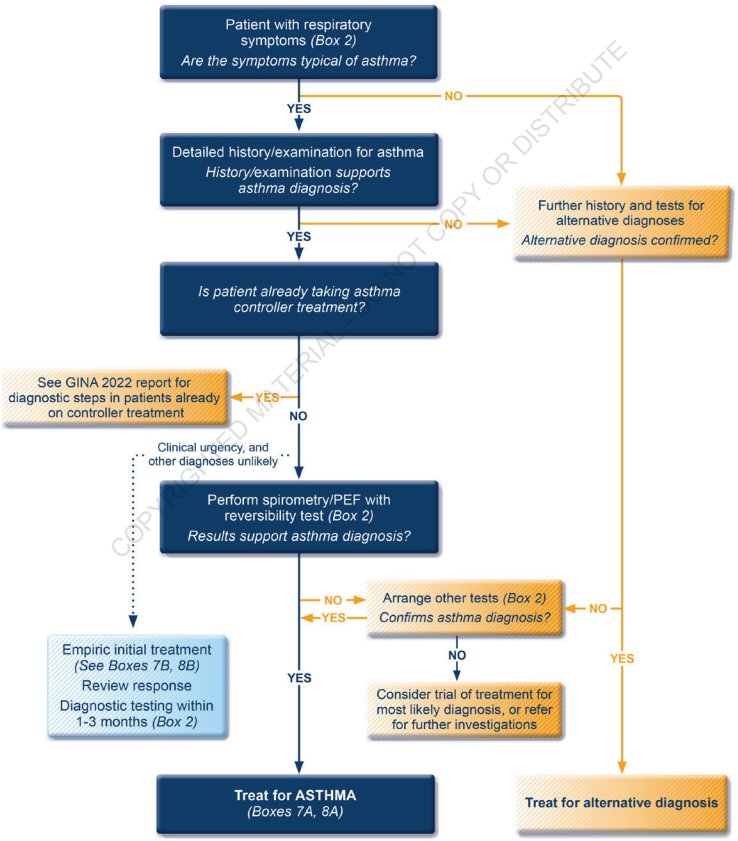
MAKING THE DIAGNOSIS OF ASTHMA

Asthma is a disease with many variations (phenotypes), usually characterized by chronic airway inflammation. Asthma has two key defining features:

- a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough, that vary over time and in intensity, AND
- variable expiratory airflow limitation, although airflow limitation may become persistent (no longer variable) in long-standing asthma.

A flowchart for making the diagnosis in clinical practice is shown in Box 1, with the specific criteria for diagnosing asthma in Box 2 (p.10).

Box 1. Diagnostic flow-chart for asthma in clinical practice



The **diagnosis of asthma should be confirmed**, and the evidence documented in the patient's medical record, preferably before starting controller treatment. Confirming the diagnosis of asthma is more difficult after treatment has been started (see p.13).

CRITERIA FOR MAKING THE DIAGNOSIS OF ASTHMA

Box 2. Features used in making the diagnosis of asthma

1. A history of variable respiratory symptoms

Typical symptoms are wheeze, shortness of breath, chest tightness, cough:

- People with asthma generally have more than one of these symptoms.
- The symptoms occur variably over time and vary in intensity.
- The symptoms often occur or are worse at night or on waking.
- Symptoms are often triggered by exercise, laughter, allergens or cold air.
- Symptoms often occur with or worsen with viral infections.

2. Evidence of variable expiratory airflow limitation

- At least once during the diagnostic process, when FEV_1 is low, document that the FEV_1/FVC ratio is below the lower limit of normal†.
- Document that variation in expiratory lung function is greater than in healthy people. For example, excess variability is recorded if:
  - FEV_1 increases after inhaling a bronchodilator by >200 mL and >12% of the pre-bronchodilator value (or in children, increases from the pre-bronchodilator value by >12% of the predicted value). This is called significant bronchodilator responsiveness or reversibility.
  - Average daily diurnal PEF variability* is >10% (in children, >13%)
  - FEV_1 increases by more than 12% and 200 mL from baseline (in children, by >12% of the predicted value) after 4 weeks of anti-inflammatory treatment (outside respiratory infections).
- The greater the variation, or the more times excess variation is seen, the more confident you can be of the diagnosis of asthma.
- Testing may need to be repeated during symptoms, in the early morning, or after withholding bronchodilator medications.
- Significant bronchodilator reversibility may be absent during severe exacerbations or viral infections. If significant bronchodilator reversibility is not present when it is first tested, the next step depends on the clinical urgency and the availability of other tests.
- For other tests to assist in diagnosis, including bronchial challenge tests, see Chapter 1 of the GINA 2022 report.

*Calculated from twice daily readings (best of 3 each time), as (the day's highest PEF minus the day's lowest PEF) divided by the mean of the day's highest and lowest PEF, and averaged over 1–2 weeks. If using PEF at home or in the office, use the same PEF meter each time. † Using Global Lung Initiative multi-ethnic reference equations.

Physical examination in people with asthma is often normal, but the most frequent finding is wheezing on auscultation, especially on forced expiration.

HOW TO CONFIRM THE DIAGNOSIS IN PATIENTS TAKING CONTROLLER TREATMENT

For many patients (25–35%) with a diagnosis of asthma in primary care, the diagnosis cannot be confirmed. If the basis of the diagnosis has not already been documented, it should be confirmed with objective testing.

If standard criteria for asthma (Box 2, p.10) are not met, consider other investigations. For example, if lung function is normal, repeat reversibility testing when the patient is symptomatic, or after withholding bronchodilators (withhold SABA for >4 hours, twice-daily ICS-LABAs for >24 hours, and once-daily ICS-LABAs for >36 hours). If the patient has frequent symptoms, consider a trial of step-up in controller treatment and repeat lung function testing after 3 months. If the patient has few symptoms, consider stepping down controller treatment; ensure the patient has a written asthma action plan, monitor them carefully, and repeat lung function testing. More information about confirming the diagnosis of asthma is in Boxes 1-3 and 1-4 of the full GINA 2022 report.

DIAGNOSING ASTHMA IN OTHER CONTEXTS

Occupational asthma and work-aggravated (work-exacerbated) asthma

Every patient with adult-onset asthma should be asked about occupational exposures, and whether their asthma is better when they are away from work. It is important to confirm the diagnosis objectively (which often needs specialist referral) and to eliminate exposure as quickly as possible.

Pregnant women

Ask all pregnant women and those planning pregnancy whether they have asthma, and advise them about the importance of taking asthma controller treatment for the health of both mother and baby.

The elderly

Asthma may be under-diagnosed in the elderly, due to poor perception, an assumption that dyspnea is normal in old age, lack of fitness, or reduced activity. Asthma may also be over-diagnosed in the elderly if shortness of breath due to heart failure or ischemic heart disease is mistakenly attributed to asthma. If there is a history of smoking or biomass fuel exposure, COPD or asthma-COPD overlap should also be considered (see below).

Smokers and ex-smokers

Asthma and COPD may co-exist or overlap (sometimes called asthma-COPD overlap [ACO] or asthma+COPD), particularly in smokers and the elderly. The history and pattern of symptoms and past records can help to distinguish asthma with persistent airflow limitation from COPD. Uncertainty about the diagnosis, or features consistent with both diagnoses, should prompt early

referral, because asthma-COPD overlap has worse outcomes than asthma or COPD alone. Asthma-COPD overlap is not a single disease, but is likely caused by several different mechanisms. There is little clinical trial evidence about how to treat these patients, as they are often excluded from clinical trials. However, patients with a diagnosis of COPD who also have any history or diagnosis of asthma should be treated with at least low dose ICS (see p.30) as well as bronchodilators, because of increased risks of hospitalization or death if they are treated with bronchodilators alone.

Patients with persistent cough as the only respiratory symptom

This may be due to chronic upper airway cough syndrome ('postnasal drip'), chronic sinusitis, gastroesophageal reflux disease (GERD), ACE-inhibitor-induced cough, inducible laryngeal obstruction (often called vocal cord dysfunction), eosinophilic bronchitis, or cough variant asthma. Cough-variant asthma is characterized by cough and airway hyperresponsiveness, and documenting variability in lung function is essential to make this diagnosis. However, lack of variability at the time of testing does not exclude asthma. For other diagnostic tests in patients with cough as their only symptom, see Box 2 (p.10), and Chapter 1 of the GINA report, or refer the patient for specialist opinion.

Diagnosis of asthma in low- and middle-income countries (LMIC)

The differential diagnosis of asthma in LMIC often includes other endemic respiratory disease (e.g. tuberculosis, HIV/AIDS-associated lung diseases, and parasitic or fungal lung diseases). A structured algorithmic approach to patients presenting with respiratory symptoms forms part of several strategies developed for improving respiratory disease management in LMIC.

Access to spirometry in LMIC is often very limited or unaffordable. In this context, PEF can be used to identify variable expiratory airflow limitation in order to confirm the diagnosis of asthma (Box 2, p.10). For example, a ≥20% improvement in PEF 15 minutes after giving 2 puffs of albuterol (salbutamol), or improved symptoms and PEF after a 4-week therapeutic trial with ICS, can help to confirm the diagnosis of asthma (or prompt investigation for alternative diagnoses) before starting long-term controller treatment.

There is a pressing need for access to affordable diagnostic tools (PEF meters and spirometry), and training in their use, to be substantially scaled up in LMIC, to avoid underdiagnosis and overdiagnosis.

ASSESSING A PATIENT WITH ASTHMA

Take every opportunity to assess patients with asthma, particularly when they are symptomatic or after a recent exacerbation, but also when they ask for a prescription refill. In addition, schedule a routine review at least once a year.

Box 3. How to assess a patient with asthma

1. Asthma control – assess both symptom control and risk factors

- Assess symptom control over the last 4 weeks (Box 4, p.14).
- Identify any modifiable risk factors for poor outcomes (Box 4, p.14).
- Measure lung function before starting treatment, 3–6 months later, and then periodically, e.g. at least yearly in most patients.

2. Are there any comorbidities?

- These include rhinitis, chronic rhinosinusitis, gastroesophageal reflux (GERD), obesity, obstructive sleep apnea, depression and anxiety.
- Comorbidities should be identified as they may contribute to respiratory symptoms, flare-ups and poor quality of life. Their treatment may complicate asthma management.

3. Treatment issues

- Record the patient's treatment. Ask about side-effects.
- Watch the patient using their inhaler, to check their technique (p.38).
- Have an open empathic discussion about adherence (p.38).
- Check that the patient has a written asthma action plan (p.42).
- Ask the patient about their goals and preferences for asthma treatment.

Box 4. Assessment of symptom control and future risk

A. Assessment of symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
Daytime symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
Any night waking due to asthma?	Yes☐ No☐			
SABA reliever needed more than twice/week?	Yes☐ No☐			
Any activity limitation due to asthma?	Yes☐ No☐			

B. Risk factors for poor asthma outcomes

Assess risk factors at diagnosis and periodically, at least every 1-2 years, particularly for patients experiencing exacerbations.
Measure FEV_1 at start of treatment, after 3–6 months for personal best lung function, then periodically for ongoing risk assessment.

Having uncontrolled asthma symptoms is an important risk factor for exacerbations

Additional potentially modifiable risk factors for exacerbations, even in patients with few asthma symptoms, include:

- *Medications*: SABA overuse (≥3x200-dose canisters/year; mortality substantially increased if ≥1 canister/month); inadequate ICS: not prescribed ICS; poor adherence; incorrect inhaler technique
- *Comorbidities*: obesity; chronic rhinosinusitis; GERD; confirmed food allergy; anxiety; depression; pregnancy
- *Exposures*: smoking; e-cigarettes; allergen exposure if sensitized; air pollution
- *Setting*: major socioeconomic problems
- *Lung function*: low FEV_1, especially if <60% predicted; high BD responsiveness
- *Type 2 inflammatory markers: high* blood eosinophils; high FeNO despite ICS treatment)

Other major independent risk factors for flare-ups (exacerbations) include:

- Ever being intubated or in intensive care for asthma; having ≥1 severe exacerbations in the last 12 months.

Having any of these risk factors increases the patient's risk of exacerbations ***even if they have few asthma symptoms***

GERD: gastroesophageal reflux disease; FeNO: exhaled nitric oxide; ICS: inhaled corticosteroid; SABA: short-acting $beta_2$-agonist. See next page for rest of table.

Box 4. Assessment of symptom control and future risk (continued)

B. Risk factors for poor asthma outcomes (continued)
Risk factors for developing persistent airflow limitation include: • History: preterm birth, low birth weight, greater infant weight gain; chronic mucus hypersecretion • Medications: lack of ICS in patients with history of severe exacerbation • Exposures: tobacco smoke, noxious chemicals, occupational exposures • Investigations: low FEV_1; sputum or blood eosinophilia
Risk factors for medication side-effects include: • *Systemic*: frequent OCS; long-term, high dose and/or potent ICS; also taking P450 inhibitors • *Local*: high dose or potent ICS; poor inhaler technique

ICS: inhaled corticosteroid; OCS: oral corticosteroid

HOW TO ASSESS ASTHMA CONTROL

Asthma control means the extent to which the effects of asthma can be seen in the patient, or have been reduced or removed by treatment. Asthma control has two domains: symptom control and risk factors for future poor outcomes, particularly flare-ups (exacerbations) (see Box 4, p.14). Questionnaires like Asthma Control Test and Asthma Control Questionnaire assess only symptom control.

Poor symptom control is a burden to patients and a risk factor for flare-ups. **Risk factors** are factors that increase the patient's future risk of having exacerbations (flare-ups), loss of lung function, or medication side-effects.

What is the role of lung function in monitoring asthma?

Once asthma has been diagnosed, lung function is most useful as an indicator of future risk. It should be recorded at diagnosis, 3–6 months after starting treatment, and periodically thereafter. Most patients should have lung function measured at least every 1–2 years, more often in children and those at higher risk of flare-ups or lung function decline. Patients who have either few or many symptoms relative to their lung function need more investigation.

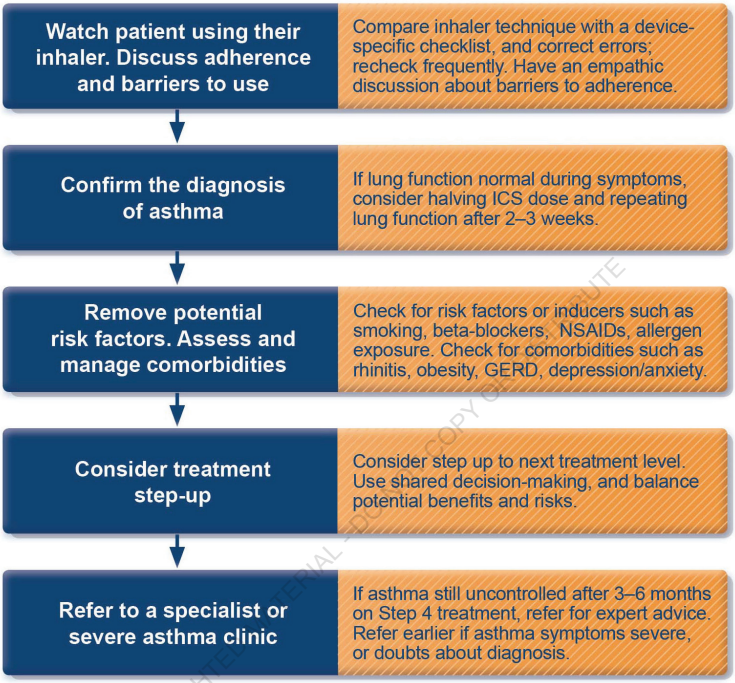
How is asthma severity assessed?

Currently, asthma severity is assessed retrospectively from the level of treatment required to control symptoms and exacerbations (i.e. after several months of treatment). Mild asthma is asthma that can be controlled with as-needed ICS-formoterol, or with low dose ICS. It is important to emphasize to patients that mild asthma still needs ICS treatment. Severe asthma is asthma that remains uncontrolled despite optimized high-dose ICS-LABA or that requires high dose ICS-LABA to prevent it from becoming uncontrolled.

HOW TO INVESTIGATE UNCONTROLLED ASTHMA

Most patients can achieve good asthma control with ICS-containing treatment, but some patients do not, and further investigation is needed.

Box 5. How to investigate uncontrolled asthma in primary care



This flowchart shows the most common problems first, but the steps can be carried out in a different order, depending on resources and clinical context.

MANAGEMENT OF ASTHMA

GENERAL PRINCIPLES

The long-term goals of asthma management are **risk reduction** and **symptom control**. The aim is to reduce the burden to the patient and to reduce their risk of asthma-related death, exacerbations, airway damage, and medication side-effects. The patient's own goals and preferences regarding their asthma and its treatment should also be identified.

Population-level recommendations about 'preferred' asthma treatments represent the overall best treatment for most patients in a particular population. For example, there are different recommendations for adults/adolescents, children 6–11 years and children 5 years and younger. In Step 5, there are also different population-level recommendations depending on the inflammatory phenotype: Type 2 or non-Type 2.

Patient-level treatment decisions should also take into account any individual characteristics, risk factors, multimorbidities or phenotype that predict how likely the patient's symptoms and exacerbation risk are to be reduced by a particular treatment, together with their personal goals, and practical issues such as inhaler technique, adherence, and affordability. For adults and adolescents, there are two treatment tracks depending on availability of medications, and on the patient's risk factors and likely adherence. More details are on p.21.

A **partnership** between the patient and their health care providers is important for effective asthma management. Training health care providers in **communication skills** may lead to increased patient satisfaction, better health outcomes, and reduced use of health care resources.

Health literacy – that is, the patient's ability to obtain, process and understand basic health information to make appropriate health decisions – should be taken into account in asthma management and education.

THE ASTHMA MANAGEMENT CYCLE TO MINIMIZE RISK AND CONTROL SYMPTOMS

Asthma management involves a continuous cycle to **assess**, **adjust treatment** and **review response** (see Box 6, p.18).

Assessment of a patient with asthma includes not only **symptom control**, but also the patient's individual **risk factors and multimorbidities** that can contribute to their burden of disease and risk of poor health outcomes, or that may predict their response to treatment. Patients (or parents of children with asthma) should be asked about their goals and preferences for asthma treatment, as part of shared decision-making about asthma treatment options.

Treatment to prevent asthma exacerbations and control symptoms includes:

Medications: GINA now recommends that every adult and adolescent with asthma should receive ICS-containing controller medication to reduce their risk of serious exacerbations, even patients with infrequent symptoms. Every patient with asthma should have a reliever inhaler for as-needed use, either low dose ICS-formoterol or SABA. ICS-formoterol is the preferred reliever because it reduces the risk of severe exacerbations compared with treatment options in which the reliever is SABA. However, ICS-formoterol should not be used as the reliever by patients who are taking a different maintenance ICS-LABA; for these patients, the appropriate reliever is SABA.

Treating modifiable risk factors and multimorbidities (Box 4, p.14)

Using **non-pharmacological therapies** and strategies as appropriate (p.39)

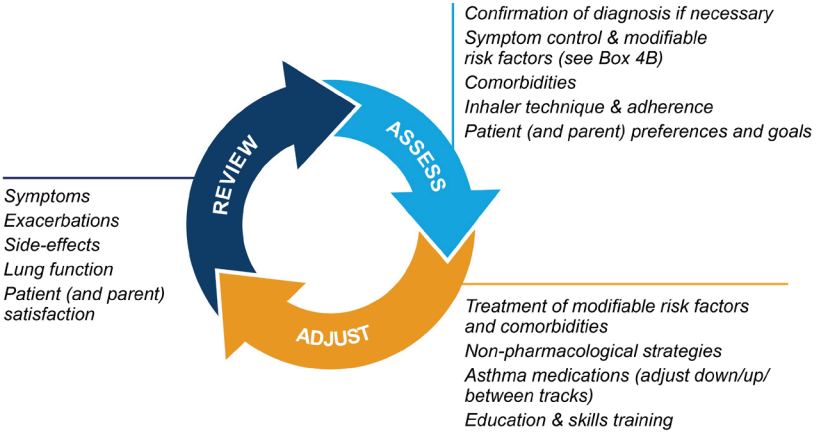
Importantly, every patient should also be trained in essential skills and guided asthma self-management, including:

- Asthma information
- Inhaler skills (p.38)
- Adherence (p.38)
- Written asthma action plan (p.42)
- Self-monitoring of symptoms and/or peak flow
- Regular medical review (p.13)

The patient's **response** should be evaluated whenever treatment is changed. Assess symptom control, exacerbations, side-effects, lung function and patient (and parent, for children with asthma) satisfaction.

Box 6. The asthma management cycle of shared decision-making

The aim of asthma management is to prevent exacerbations and asthma deaths, and to relieve and control symptoms.



GINA RECOMMENDATIONS FOR MILD ASTHMA

For safety, GINA does not recommend treatment of asthma in adults and adolescents with short-acting beta$_2$-agonists (SABA) alone, without inhaled corticosteroids (ICS). There is strong evidence that SABA-only treatment, although providing short-term relief of asthma symptoms, does not protect patients from severe exacerbations, and that regular or frequent use of SABA increases the risk of exacerbations.

Instead, GINA recommends that all adults and adolescents with asthma should receive ICS-containing controller treatment to reduce their risk of serious exacerbations and to control symptoms.

For adults and adolescents, the treatment options for mild asthma are:

- as-needed low dose ICS-formoterol (preferred), or
- regular low dose ICS, plus as-needed SABA.

Why did GINA change its recommendations in 2019?

The new recommendations in GINA 2019 represented the culmination of a 12-year campaign by GINA to obtain evidence for new strategies for treatment of mild asthma. Our aims were:

- to reduce the risk of asthma-related exacerbations and death, including in patients with so-called mild asthma
- to provide consistent messaging about the aims of treatment, including prevention of exacerbations, across the spectrum of asthma severity
- to avoid establishing a pattern of patient reliance on SABA early in the course of the disease.

Additional information is provided on page 31 about the evidence and rationale for each of the recommendations in Steps 1 and 2.

Why are there concerns about SABA-only treatment?

Many guidelines recommend that patients with mild asthma should be treated with as-needed SABA reliever alone. This dates back more than 50 years, to when asthma was thought of primarily as a disease of bronchoconstriction. However, airway inflammation is found in most patients with asthma, even in those with intermittent or infrequent symptoms.

Although SABA provides quick relief of symptoms, SABA-only treatment is associated with increased risk of exacerbations and lower lung function. *Regular use of SABA* increases allergic responses and airway inflammation, and reduces the bronchodilator response to SABA when it is needed. *Over-use of SABA* (e.g. ≥3 x 200-dose canisters dispensed in a year) is associated with an increased risk of severe exacerbations. Dispensing of ≥12 SABA canisters in a year (and possibly even less than this) is associated with increased risk of asthma-related death.

STARTING ASTHMA TREATMENT

For the best outcomes, **ICS-containing treatment should be initiated** as soon as possible after the diagnosis of asthma is made, because:

- Patients with even mild asthma can have severe exacerbations
- Low dose ICS markedly reduces asthma hospitalizations and death
- Low dose ICS is very effective in preventing severe exacerbations, reducing symptoms, improving lung function, and preventing exercise-induced bronchoconstriction, even in patients with mild asthma
- Early treatment with low dose ICS is associated with better lung function than if symptoms have been present for more than 2–4 years
- Patients not taking ICS who experience a severe exacerbation have lower long-term lung function than those who have started ICS
- In occupational asthma, early removal from exposure and early treatment increase the probability of recovery.

For most adults or adolescents with asthma, treatment can be started at Step 2 with either as-needed low dose ICS-formoterol (preferred), or regular daily low dose ICS with as-needed SABA. See Box 7B, p.24.

Most patients with asthma do not need higher doses of ICS, because at a group level, most of the benefit (including prevention of exacerbations) is obtained at low doses. For ICS doses, see Box 9, p.30.

Consider starting at Step 3 (e.g. maintenance and reliever therapy with low dose ICS-formoterol) if, at initial presentation, the patient has troublesome asthma symptoms most days (e.g. 4–5 days/week); or is waking from asthma once or more a week.

If the patient has severely uncontrolled asthma at initial asthma presentation, or the initial presentation is during an acute exacerbation, start regular controller treatment at Step 4 (e.g. medium dose ICS-formoterol maintenance and reliever therapy); a short course of OCS may also be needed.

Consider stepping down after asthma has been well-controlled for 3 months. However, in adults and adolescents, ICS should not be completely stopped.

Before starting initial controller treatment (Box 7B, p.24 and 8B, p.28)

- Record evidence for the diagnosis of asthma.
- Document symptom control and risk factors.
- Assess lung function, when possible.
- Train the patient to use the inhaler correctly, and check their technique.
- Schedule a follow-up visit.

After starting initial controller treatment (Box 7A, p.22, and 8A, p.26)

- Review response after 2–3 months, or according to clinical urgency.
- See Box 7A/8A for ongoing treatment and other key management issues.
- Consider step-down when asthma has been well controlled for 3 months.

ASTHMA TREATMENT TRACKS FOR ADULTS & ADOLESCENTS

The options for ongoing treatment for adults and adolescents have been clarified in the main treatment figure (Box 7A, p.22) by showing two treatment 'tracks'. The key difference between the tracks is the medication that is used for symptom relief: as-needed low dose ICS-formoterol in Track 1 (preferred), and as-needed SABA in Track 2.

***Track 1*: The reliever is as-needed low dose ICS-formoterol.**
This is the preferred approach recommended by GINA for adults and adolescents, based on strong evidence that it reduces the risk of severe exacerbations compared with regimens with SABA as reliever, with similar symptom control. With this approach:

- When a patient at any treatment step has asthma symptoms, they use low dose ICS-formoterol in a single inhaler for symptom relief.
- In Steps 3–5, patients also take ICS-formoterol as their regular daily treatment. This is called 'maintenance and reliever therapy' (MART).

ICS-formoterol should not be used as the reliever by patients taking any other (non-formoterol) ICS-LABA.

***Track 2*: The reliever is as-needed SABA.** This is an alternative approach when Track 1 is not possible or is not preferred by a patient who has stable asthma and no exacerbations on their current therapy.

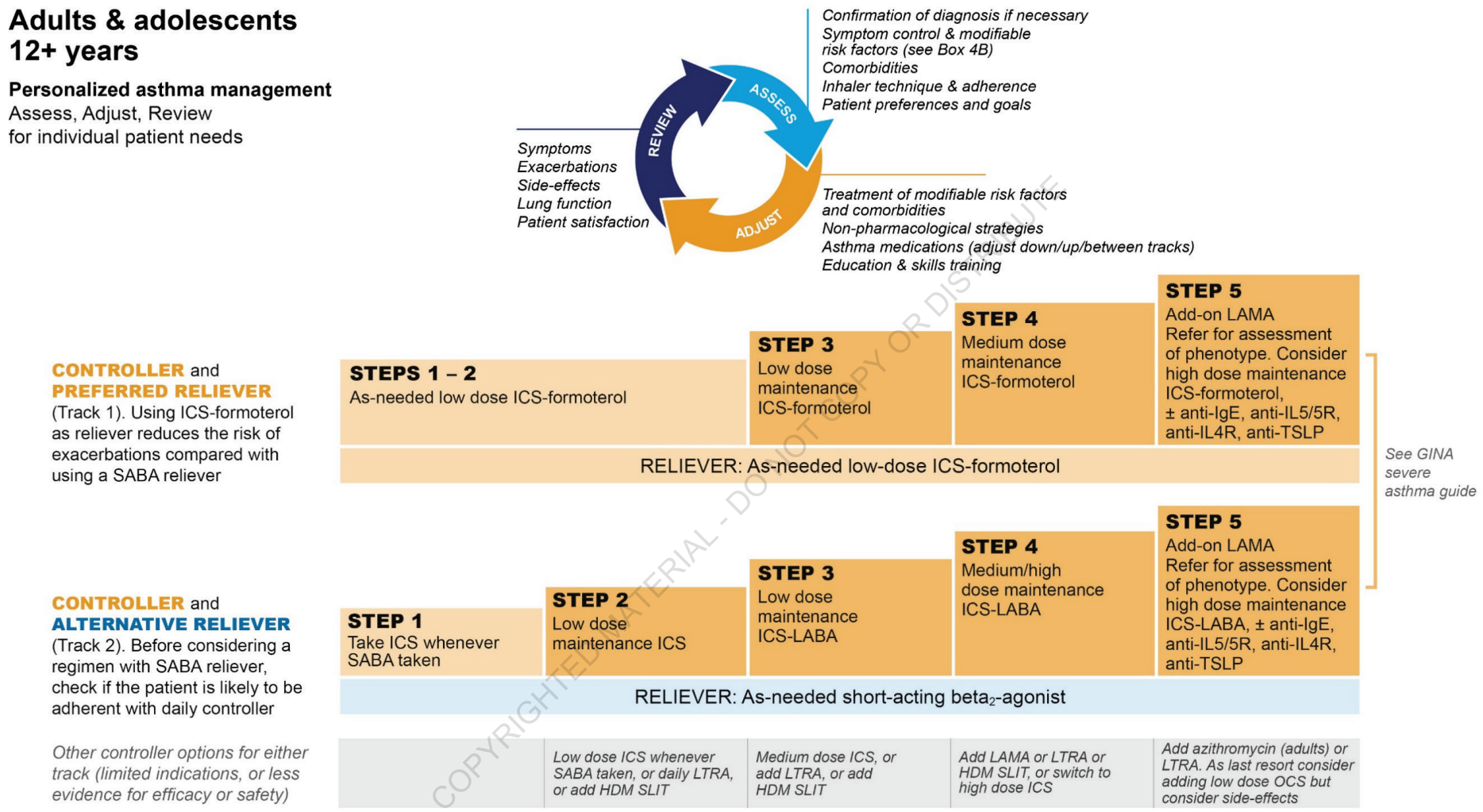
- In Step 1, the patient takes a SABA and a low dose ICS together for symptom relief when symptoms occur, either in a combination inhaler, or with the ICS taken right after the SABA.
- In Steps 2–5, a SABA (alone) is used for symptom relief, and the patient takes ICS-containing controller medication regularly every day.

However, before prescribing a regimen with SABA reliever, consider whether the patient is likely to be adherent with their ICS-containing controller therapy, as otherwise they will be exposed to SABA-only treatment and a higher risk of exacerbations.

During ongoing treatment, treatment can be stepped up or down along one track, using the same reliever at each step, or it can be switched between tracks, according to the individual patient's needs.

Before stepping up, check for common problems such as incorrect inhaler technique, poor adherence, and environmental exposures, and confirm that the symptoms are due to asthma (see Box 5, p.16) .

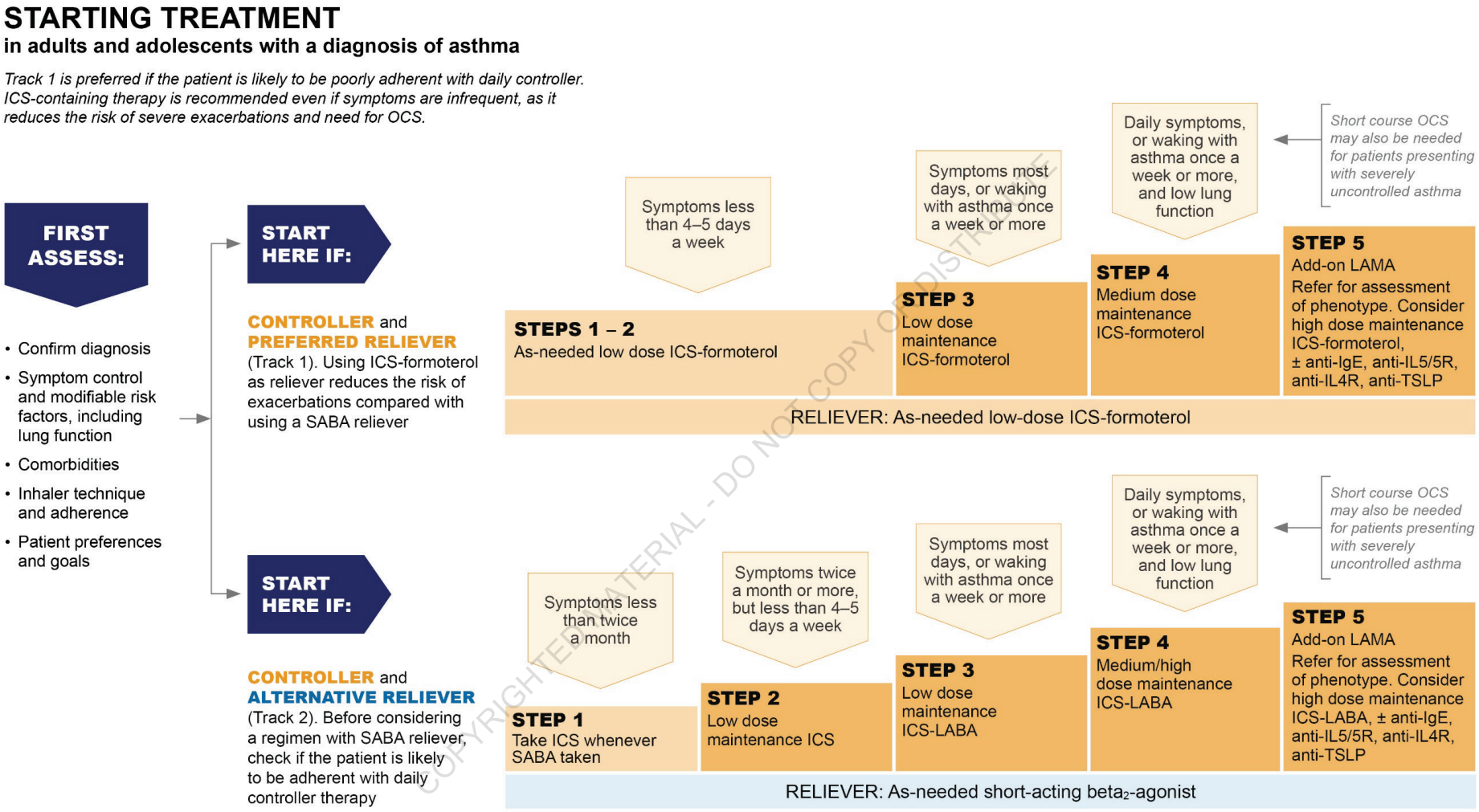
Box 7A. The GINA asthma treatment strategy – adults and adolescents



ICS: inhaled corticosteroid; LABA: long-acting beta$_2$-agonist; LAMA: long-acting muscarinic antagonist; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid; SABA: short-acting beta$_2$-agonist

See Box 8A (p.26) for children 6–11 years. For more details about treatment recommendations, and for supporting evidence, and clinical advice about implementation in different populations see the full GINA 2022 report (www.ginasthma.org). For more details about Step 5 add-on therapies, see Chapter 3E of the GINA report or the GINA 2022 Short Guide on Difficult to Treat and Severe Asthma, and check eligibility criteria with local payers.

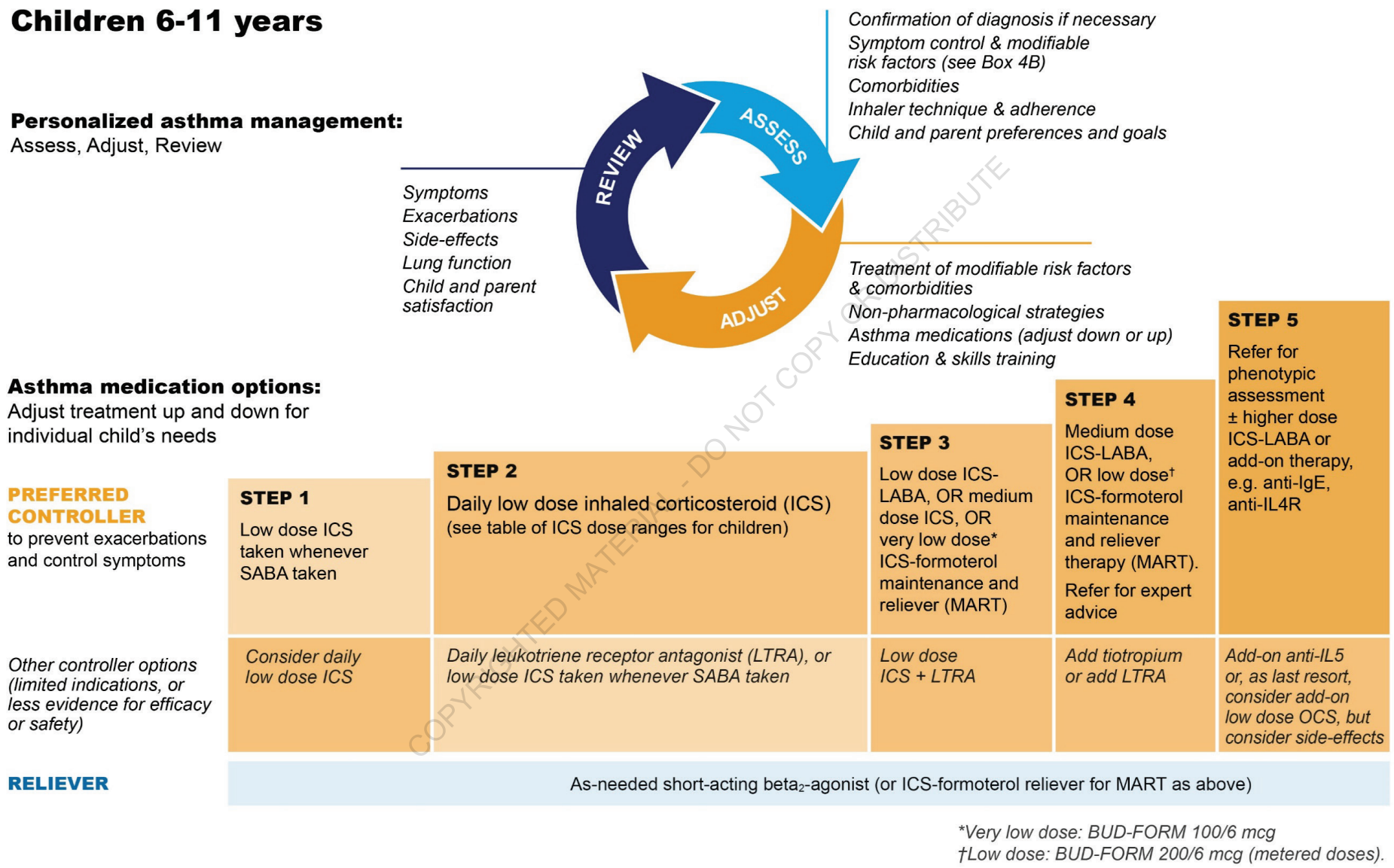
Box 7B. Initial treatment: adult or adolescents with a diagnosis of asthma



ICS: inhaled corticosteroid; SABA: short-acting beta$_2$-agonist

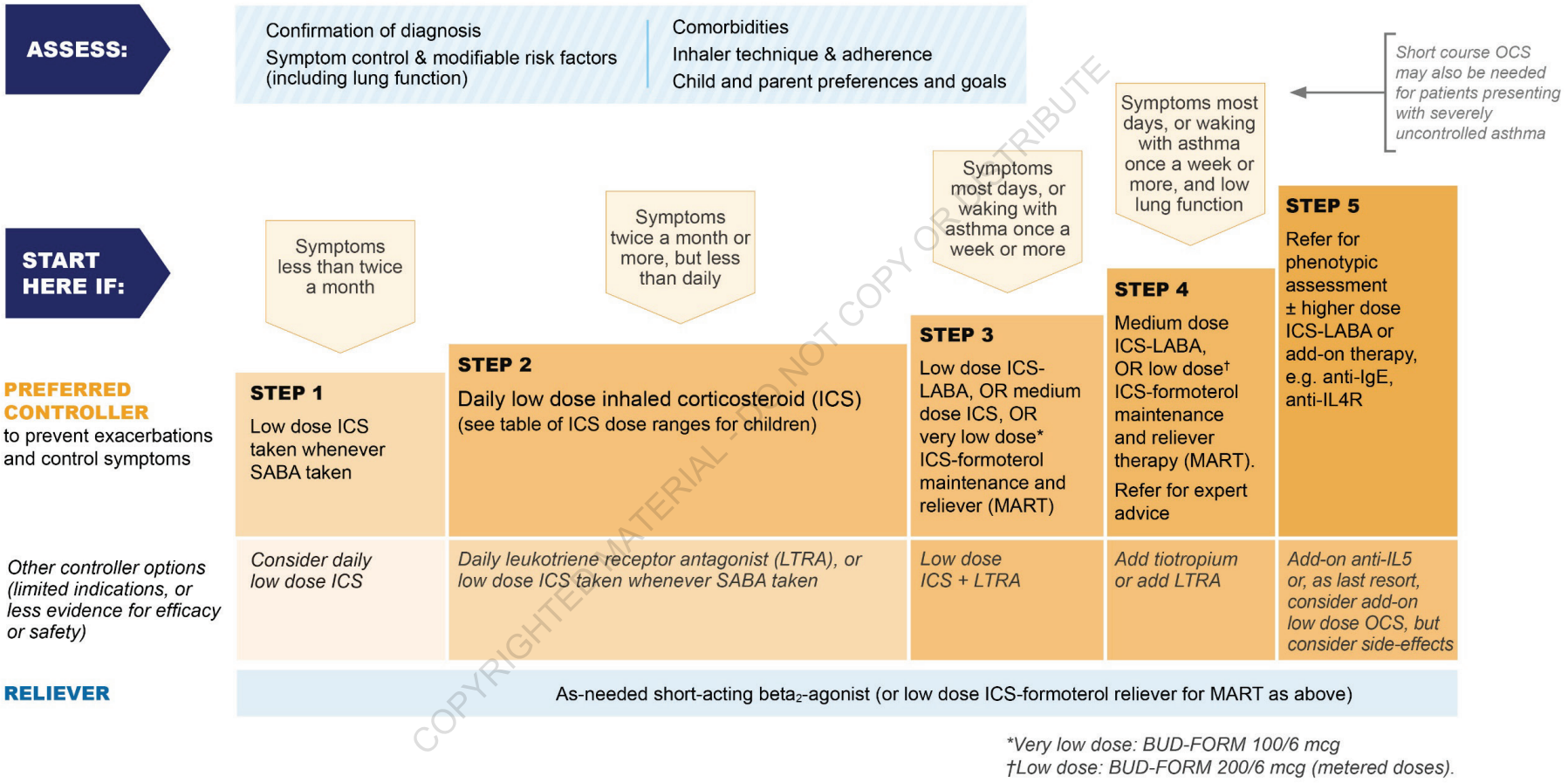
For initial asthma treatment in children 6–11 years, see Box 8B (p.28). For more details about treatment recommendations including supporting evidence, and clinical advice about implementation in different populations see the full GINA 2022 report (www.ginasthma.org). For more details about Step 5 add-on therapies, see Chapter 3E of the GINA report, or the GINA 2022 Short Guide on Difficult to Treat and Severe Asthma, and check eligibility criteria with local payers.

Box 8A. The GINA asthma treatment strategy – children 6–11 years



ICS: inhaled corticosteroid; LABA: long-acting beta$_2$-agonist; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid; SABA: short-acting beta$_2$-agonist.
See Box 7A (p.22) for adults and adolescents. For more details about treatment recommendations, and for supporting evidence, and clinical advice about implementation in different populations see the full GINA 2022 report (www.ginasthma.org). Check eligibility criteria with local payers.

Box 8B. Initial treatment: children 6–11 years with a diagnosis of asthma



ICS: inhaled corticosteroid; LABA: long-acting beta$_2$-agonist; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid; SABA: short-acting beta$_2$-agonist.
For initial asthma treatment in adults and adolescents, see Box 7B (p.24). For more details about treatment recommendations including supporting evidence, and clinical advice about implementation in different populations see the full GINA 2022 report (www.ginasthma.org). Check eligibility criteria with local payers.

Box 9. Low, medium and high daily doses of inhaled corticosteroids

This is not a table of equivalence, but suggested total daily ICS doses for the 'low', 'medium' and 'high' dose options in Boxes 7 and 8. It is based on available studies and product information. Doses may be country-specific depending on local availability, regulatory labelling and clinical guidelines, and for mometasone, with addition of LAMA to ICS-LABA.

Low dose ICS provides most of the clinical benefit for most patients. However, ICS responsiveness varies between patients, so some patients may need **medium dose ICS** if asthma is uncontrolled despite good adherence and correct inhaler technique with low dose ICS.
High dose ICS is needed by very few patients, and its long-term use is associated with an increased risk of local and systemic side-effects.

Adults and adolescents	**Total daily ICS dose (mcg)**		
Inhaled corticosteroid	**Low**	**Medium**	**High**
BDP (pMDI*, HFA)	200–500	>500–1000	>1000
BDP (DPI or pMDI, extrafine particle, HFA)	100–200	>200–400	>400
Budesonide (DPI or pMDI*, HFA)	200–400	>400–800	>800
Ciclesonide (pMDI, extrafine particle, HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100		200
Fluticasone propionate (DPI)	100–250	>250–500	>500
Fluticasone propionate (pMDI*, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	Depends on DPI device		
Mometasone furoate (pMDI*, HFA)	200–400		400
Children 6–11 years	**Total daily ICS dose (mcg)**		
Inhaled corticosteroid	**Low**	**Medium**	**High**
BDP (pMDI*, HFA)	100–200	>200–400	>400
BDP (pMDI, extrafine particle, HFA)	50–100	>100–200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide (pMDI, extrafine particle, HFA)	80	>80–160	>160
Fluticasone furoate (DPI)	50		n.a.
Fluticasone propionate (DPI)	50–100	>100–200	>200
Fluticasone propionate (pMDI*, HFA)	50–100	>100–200	>200
Mometasone furoate (pMDI*, HFA)	100		200

BDP: beclometasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler. Table shows metered doses.
* standard (non-fine) particle. ICS by pMDI should preferably be used with a spacer..

For new or generic preparations, or products containing a LAMA, the manufacturer's product Information should be reviewed carefully, as products containing the same molecule may not be clinically equivalent.

STEPWISE APPROACH FOR ADJUSTING TREATMENT FOR INDIVIDUAL PATIENT NEEDS

For clarity, treatment options for adults and adolescents in Box 7A (p.22) are shown as two tracks, based on the choice of reliever. In Track 1, the reliever is low dose ICS-formoterol. This is the preferred approach recommended by GINA, because it reduces the risk of severe exacerbations compared with using a SABA reliever (as in Track 2).

Once asthma treatment has been started (Box 7B, p.24 and Box 8B, p.28), ongoing decisions are based on a cycle of shared decision-making to assess the patient, adjust their treatment (pharmacological and non-pharmacological) if needed, and review their response (Box 6, p.18). Treatment can be stepped up or down along one track using the same reliever at each step, or it can be switched between tracks, according to the individual patient's needs.

The **preferred controller treatments** at each step are shown in Box 7A (p.22) for adults and adolescents and in Box 8A (p.26) for children 6–11 years. See Box 9 (p.30) for ICS doses. For more details, including for children 5 years and younger, see the full GINA 2022 report.

At each step, **other controller options** are also listed, that have specific indications or less evidence for efficacy and safety.

For patients whose asthma is not well controlled on a particular treatment, adherence, inhaler technique and comorbidities should be checked before considering a different medication in the same step, or before stepping up.

STEP 1. Preferred treatment for adults and adolescents: low dose ICS-formoterol taken as needed for symptom relief (Track 1)

Step 1 recommendations are for:

- Initial asthma treatment for patients with symptoms less than twice a month and no exacerbation risk factors, a group that is rarely studied
- Step-down treatment for patients whose asthma is well controlled on Step 2 treatment

As-needed low dose ICS-formoterol is the preferred treatment for adult and adolescent patients with mild asthma. This strategy is supported by evidence from two studies comparing as-needed budesonide-formoterol with SABA-only treatment in patients eligible for Step 2 therapy (see below).

In making this recommendation, the most important considerations were that:

- Patients with few interval asthma symptoms can have severe or fatal exacerbations
- The historic distinction between so-called 'intermittent' and 'persistent' asthma is arbitrary. With as-needed ICS-formoterol, a large reduction in risk of severe exacerbations was seen compared with as-needed SABA,

even in patients with SABA use twice a week or less at baseline.
- Adherence with daily ICS is particularly poor in patients with infrequent symptoms, exposing them to risks of SABA-only treatment.
- There is no evidence for the safety or efficacy of SABA-only treatment. Regular use of SABA for 1–2 weeks leads to increased airway hyper-responsiveness and reduced bronchodilatation. SABA over-use (e.g. dispensing of 3 or more 200-dose canisters/year) is associated with increased risk of exacerbations and death.
- It is important to avoid the conflicting messages from the past in which patients were initially told to use SABA for symptom relief but then (despite this treatment being effective from their perspective) they were told that they needed to take a daily controller to reduce their SABA use and prevent exacerbations. Starting treatment with SABA alone trains the patient to regard SABA as their primary asthma treatment.

All evidence for as-needed ICS-formoterol so far is with low dose budesonide-formoterol, but beclometasone-formoterol may also be suitable. Both of these medications are well-established to reduce exacerbations with maintenance and reliever therapy in Steps 3 to 5, and no new safety signals were seen in the studies with as-needed budesonide-formoterol in mild asthma.

The usual dose of as-needed budesonide-formoterol in mild asthma is one inhalation of 200/6 mcg (delivered dose 160/4.5 mcg) taken whenever needed for symptom relief, or before exercise if needed. The maximum recommended dose in a single day is a total of 72 mcg formoterol (54 mcg metered dose). However, in the mild asthma studies, patients rarely needed this much, and average usage was only 3–4 inhalations per week.

Other controller options at Step 1 for adults and adolescents (Track 2)

Low dose ICS taken whenever SABA is taken: This may be an option if as-needed ICS-formoterol is not available or affordable, although there is much less evidence for its safety and effectiveness. In Step 1, the evidence is indirect, from studies with separate or combination ICS and SABA inhalers in patients with well-controlled asthma on Step 2 treatment (see below). For this recommendation, the most important considerations were reducing the risk of severe exacerbations, and the fact that adherence with daily ICS is poor in patients with symptoms less than twice a month.

Daily low dose ICS is no longer recommended at Step 1, since patients with symptoms less than twice a month are unlikely to take ICS regularly, leaving them exposed to the risks of SABA-only treatment.

Children 6–11 years

Taking ICS whenever SABA is taken is a possible option, with indirect evidence from two Step 2 studies with separate ICS and SABA inhalers.

STEP 2. Preferred treatment for adults and adolescents: low dose ICS-formoterol taken as needed for symptom relief (Track 1)

As-needed low dose ICS-formoterol taken for symptom relief: the evidence to date in mild asthma is with low dose budesonide-formoterol.

- Compared with as-needed SABA alone, as-needed ICS-formoterol reduces severe exacerbations by 60–64% and ED/hospital visits by 65%.
- Compared with daily low dose ICS, as-needed ICS-formoterol reduces severe exacerbations to a similar extent, and reduces ED/hospital visits by 37%, with a very small difference in symptom control favoring ICS.
- Even a single day with increased as-needed doses of ICS-formoterol reduces the short-term risk of severe exacerbations compared with SABA alone, suggesting that timing of use is important
- The treatment effects with as-needed ICS-formoterol compared with SABA alone or daily ICS were similar regardless of whether blood eosinophils or FeNO were low or elevated.

For this recommendation in patients with mild asthma, the most important considerations were to prevent severe exacerbations and to avoid the need for daily ICS. The small differences in symptom control and lung function, compared with daily ICS, were considered to be less important, as they were much less than the minimal important difference.

The usual dose of as-needed budesonide-formoterol is one inhalation of 200/6 mcg (delivered dose 160/4.5 mcg) taken whenever needed for symptom relief. The maximum recommended dose in a single day is a total of 72 mcg formoterol (delivered dose 48 mcg). In mild asthma studies, average usage was only 3–4 inhalations per week.

ICS-formoterol taken as-needed and before exercise showed similar benefit as daily ICS. This suggests that patients prescribed as-needed ICS-formoterol do not need to be prescribed a SABA for pre-exercise use.

Alternative Step 2 treatment for adults and adolescents: daily low dose ICS plus as-needed SABA (Track 2)

There is a large body of evidence from RCTs and observational studies showing that the risks of severe exacerbations, hospitalizations and mortality are substantially reduced with regular low dose ICS. Symptoms and exercise-induced bronchoconstriction are also reduced. Severe exacerbations are halved even in patients with symptoms 0–1 days a week. For this recommendation, the most important consideration was reducing the risk of severe exacerbations. However, adherence with ICS in the community is very poor, exposing patients to the risks of SABA-only treatment.

Other controller options at Step 2

- *Low dose ICS taken whenever SABA is taken,* in combination or separate inhalers. Evidence is from two studies in adults and two studies in children/adolescents, showing no difference in exacerbations compared with daily ICS. A high importance was given to preventing severe exacerbations, and a lower importance was given to small differences in symptom control and the inconvenience of needing to carry two inhalers.
- *Leukotriene receptor antagonists (LTRA)* are less effective than daily ICS, particularly for preventing exacerbations. There is a US FDA boxed warning about the risk of serious mental health effects with montelukast.
- *Daily low dose ICS-LABA* as initial therapy leads to faster improvement in symptoms and FEV_1 than ICS alone but is costlier, and the reduction in exacerbations compared with SABA is similar to that with ICS.
- For purely seasonal allergic asthma, evidence is needed. Current advice is to start ICS or as-needed ICS-formoterol at the start of the allergen season and cease 4 weeks after end of exposure.
- For adults with rhinitis who are allergic to house dust mite and have FEV_1 >70% predicted, consider adding sublingual immunotherapy (SLIT).

Step 2 treatment for children 6–11 years

The preferred controller option is regular low dose ICS with as-needed SABA (see Box 9, p.30 for ICS doses). Other options include taking low dose ICS whenever SABA is taken, using separate inhalers. Daily LTRA is less effective for exacerbation reduction; advise parents about FDA warning.

STEP 3. Preferred treatment for adults and adolescents: low dose ICS-formoterol maintenance and reliever therapy (Track 1)

Before considering a step-up in treatment, check adherence, inhaler technique, environmental exposures, and comorbidities.

The preferred Step 3 option is low dose ICS-formoterol as both maintenance and reliever treatment (MART). In patients with or without a history of severe exacerbations, this reduces the risk of severe exacerbations compared with other options (maintenance ICS-LABA, higher dose ICS, or conventional best practice) with as-needed SABA, with a similar level of symptom control.

The maximum recommended dose of ICS-formoterol in a single day is a *total* of 48 mcg formoterol for BDP-formoterol (36 mcg delivered dose), and 72 mcg formoterol for budesonide-formoterol (54 mcg delivered dose).

Alternative Step 3 treatment for adults and adolescents: maintenance low dose ICS-LABA plus as-needed SABA (Track 2)

For patients whose asthma is uncontrolled on low dose ICS, low dose combination ICS-LABA reduces severe exacerbations by about 20%, and lung function is higher, with little difference in reliever use.

Other controller options for adults and adolescents: Medium dose ICS, or low dose ICS plus LTRA (but see above re FDA warning). For adults with rhinitis who are allergic to house dust mite and have FEV_1 >70% predicted, consider adding sublingual immunotherapy (SLIT).

Preferred Step 3 treatment for children 6–11 years

After checking inhaler technique and adherence, and treating modifiable risk factors, there are three preferred options for children:

- Medium dose ICS with as-needed SABA (see Box 9, p.30, for ICS doses)
- Low dose ICS-LABA, with as-needed SABA. Combination ICS-LABA is non-inferior to ICS alone for severe exacerbations, with no difference in symptom control or reliever use
- Maintenance and reliever therapy with a very low dose of budesonide-formoterol (100/6 mcg once-daily, 80/4.5 mcg delivered dose) showed a large reduction in severe exacerbations in children compared with the same dose of ICS-formoterol or higher dose of ICS.

Individual children's responses vary, so each of these options may be tried before considering a step-up.

STEP 4. Preferred treatment for adults and adolescents: Medium dose ICS-formoterol as maintenance and reliever therapy (Track 1)

At a group level, most benefit from ICS is obtained at low dose, but individual ICS responsiveness varies, and some patients whose asthma is uncontrolled on Step 3 MART despite good adherence and correct technique may benefit from increasing the maintenance ICS-formoterol dose to medium.

The maintenance dose can be increased by doubling the number of maintenance inhalations. However, the reliever should still be *low* dose ICS-formoterol. The maximum recommended dose in a single day is the same as in Step 3.

Alternative Step 4 treatment for adults and adolescents: medium or high dose ICS-LABA with as-needed SABA (Track 2)

Some patients whose asthma is uncontrolled or who have frequent exacerbations on low dose ICS-LABA despite good adherence and correct technique may benefit from medium dose ICS-LABA, if MART is not available.

Other Step 4 controller options for adults and adolescents include add-on LAMA for patients ≥18 years (≥6 years for tiotropium by mist inhaler) in separate or combination ('triple') inhalers. Compared with ICS-LABA, there is a modest increase in lung function, and a small decrease in exacerbations, but no clinically important reduction in symptoms. Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium,

or switch to MART. For adult patients with rhinitis and asthma who are allergic to house dust mite, consider adding SLIT, provided FEV_1 is >70% predicted.

***Preferred Step 4 treatment for children (6–11 years)**:* Options include increasing the dose of maintenance ICS-LABA to medium; for maintenance and reliever therapy, the maintenance dose may be increased to 100/6 mcg twice daily (metered dose 80/4.5 mcg). If asthma is not well controlled with Step 4 treatment, continue controller, and refer for expert advice.

STEP 5. Refer for phenotypic investigation ± add-on treatment

Patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma inflammatory phenotype, and potential add-on treatment. The GINA short guide *Difficult to Treat and Severe Asthma* v4.0 2022 provides a decision tree and practical guide for assessment and management in adults and adolescents. Treatment guided by sputum eosinophils, if available, reduces exacerbations in moderate-severe asthma. There is no evidence about initiating MART in patients taking Step 5 add-on treatment, but for a patient on MART, switching the reliever back to SABA may increase exacerbation risk.

Add-on treatments in Step 5 include LAMA for patients ≥18 years (≥6 years for tiotropium) in separate or combination ('triple') inhalers; anti-IgE (SC omalizumab, ≥6 years) for severe allergic asthma; anti-IL5 (SC mepolizumab, ≥6 years, or IV reslizumab, ≥18 years) or anti-IL5R (SC benralizumab, ≥12 years) or anti-IL4R (SC dupilumab, ≥6 years) for severe eosinophilic asthma; and anti-TSLP (SC tezepelumab, ≥12 years) for severe asthma. See glossary (p.46) and always check local eligibility criteria for specific add-on therapies. Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance.

Other options: Maintenance OCS should be used only as last resort, because short-term and long-term systemic side-effects are common and serious.

REVIEWING RESPONSE AND ADJUSTING TREATMENT

How often should patients with asthma be reviewed?

Patients should preferably be seen 1–3 months after starting treatment and every 3–12 months after that, but in pregnancy, asthma should be reviewed every 4–6 weeks. After an exacerbation, a review visit within 1 week should be scheduled. The frequency of review depends on the patient's initial level of symptom control, their risk factors, their response to initial treatment, and their ability and willingness to engage in self-management with an action plan.

Stepping up asthma treatment

Asthma is a variable condition, and periodic adjustment of controller treatment by the clinician and/or patient may be needed.

- *Sustained step-up (for at least 2–3 months)*: if symptoms and/or exacerbations persist despite 2–3 months of controller treatment, assess the following common issues before considering a step-up
  - incorrect inhaler technique
  - poor adherence
  - modifiable risk factors, e.g. smoking
  - are symptoms due to comorbid conditions, e.g. allergic rhinitis
- *Short-term step-up (for 1–2 weeks)* by clinician or by patient with written asthma action plan (p.42), e.g. during viral infection or allergen exposure
- *Day-to-day adjustment by patient in GINA Track 1* (p.22), with as-needed low dose ICS-formoterol for mild asthma, or ICS-formoterol as maintenance and reliever therapy (MART) for moderate-severe asthma. This is particularly effective in reducing severe exacerbations.

Stepping down treatment when asthma is well-controlled

Consider stepping down treatment once good asthma control has been achieved and maintained for 2–3 months, to find the lowest treatment that controls both symptoms and exacerbations, and minimizes side-effects:

- Choose an appropriate time for step-down (no respiratory infection, patient not travelling, not pregnant).
- Assess risk factors, including history of previous exacerbations or emergency department visit, and low lung function.
- Document baseline status (symptom control and lung function), provide a written asthma action plan, monitor closely, and book a follow-up visit.
- Step down through available formulations to reduce the ICS dose by 25–50% at intervals of 2–3 months (see Box 3-7 in full GINA 2022 report for details of how to step down different controller treatments).
- If asthma is well controlled on low dose ICS or LTRA, as-needed low dose ICS-formoterol is a step-down option, based on three large studies in mild asthma. Smaller studies have also shown that low dose ICS taken whenever SABA is taken (with combination or separate inhalers) is more effective as a step-down strategy than SABA alone.
- Do not completely stop ICS in adults or adolescents with asthma unless this is needed temporarily to confirm the diagnosis of asthma.
- Make sure a follow-up appointment is arranged.

INHALER SKILLS AND ADHERENCE

Provide skills training for effective use of inhaler devices

Most patients (up to 80%) cannot use their inhaler correctly. This contributes to poor symptom control and exacerbations, and increases the risk of local adverse effects. To ensure effective inhaler use:

- **Choose** the most appropriate device for the patient before prescribing: consider medication, physical problems e.g. arthritis, patient skills, and cost; for ICS by pressurized metered dose inhaler, prescribe a spacer.
- **Check** inhaler technique at every opportunity. Ask the patient to show you how they use the inhaler. Check against a device-specific checklist.
- **Correct** using a physical demonstration, paying attention to incorrect steps. Check technique again, up to 2–3 times if necessary.
- **Confirm** that you have checklists for each of the inhalers you prescribe, and can demonstrate correct technique on them.

More information can be found on the GINA website (www.ginasthma.org) and the ADMIT website (www.inhalers4u.org).

Check and improve adherence with asthma medications

At least 50% of adults and children do not take controller medications as prescribed. Poor adherence, with reliance on SABA reliever, contributes to poor symptom control and exacerbations. It may be unintentional (e.g. forgetfulness, cost, misunderstandings) and/or intentional (e.g. not perceiving the need for treatment, fear of side-effects, cultural issues, cost).

Identify patients with adherence problems:

- Ask an empathic question, e.g. "*Most patients don't take their inhaler exactly as prescribed. In the last 4 weeks, how many days a week have you been taking it? 0 days a week, or 1, or 2 days [etc]?*", or "*Do you find it easier to remember your inhaler in the morning or night?*"
- Check medication usage, from prescription date, inhaler date/dose counter, dispensing records
- Ask patients about attitudes and beliefs about asthma and medications

Only a few adherence interventions have been studied closely in asthma and have led to improved adherence in real-world studies:

- Shared decision-making for medication and dose choice
- Inhaler reminders for missed doses
- Comprehensive asthma education with home visits by asthma nurses
- Clinicians reviewing feedback about their patients' dispensing records
- An automated voice recognition program with telephone messages triggered when refills were due or overdue
- Directly-observed controller therapy at school, with telemedicine oversight.

TREATING MODIFIABLE RISK FACTORS

Exacerbation risk can be minimized by optimizing asthma medications, and by identifying and treating modifiable risk factors. Some examples of risk modifiers with consistent high-quality evidence are:

- **Guided self-management**: self-monitoring of symptoms and/or PEF, a written asthma action plan (p.42), and regular medical review
- **Use of a regimen that minimizes exacerbations**: prescribe an ICS-containing controller, either daily, or, for mild asthma, as-needed ICS-formoterol. GINA Track 1 (p.22), with ICS-formoterol as the reliever (with maintenance ICS-formoterol in MART, or alone in mild asthma) reduces the risk of severe exacerbations compared with if the reliever is SABA
- **Avoidance of exposure to tobacco smoke**
- **For confirmed food allergy**: appropriate food avoidance; ensure availability of injectable epinephrine for anaphylaxis
- **School-based programs** that include asthma self-management skills
- **Referral to a specialist center**, if available, for patients with severe asthma, for detailed assessment and consideration of add-on biologic medications and/or sputum-guided treatment.

NON-PHARMACOLOGICAL STRATEGIES AND INTERVENTIONS

In addition to medications, other therapies and strategies may be considered where relevant, to assist in symptom control and risk reduction. See GINA 2022 Box 3-9 for details. Some examples with consistent high-quality evidence include:

- **Smoking cessation advice**: at every visit, strongly encourage smokers to quit. Provide access to counselling and resources. Advise parents and carers to exclude smoking in rooms/cars used by children with asthma
- **Physical activity**: encourage people with asthma to engage in regular physical activity because of its general health benefits; it may also have a small benefit for asthma control and lung function. Provide advice about management of exercise-induced bronchoconstriction.
- **Investigation for occupational asthma**: ask all patients with adult-onset asthma about their work history. Identify and remove occupational sensitizers as soon as possible. Refer for expert advice, if available.
- **Identify aspirin-exacerbated respiratory disease**, and before prescribing NSAIDs including aspirin, always ask about previous reactions .

Although allergens may contribute to asthma symptoms in sensitized patients, allergen avoidance is not recommended as a general strategy for asthma. These strategies are often complex and expensive, and there are no validated methods for identifying those who are likely to benefit.

Some common triggers for asthma symptoms (e.g. exercise, laughter) should **not** be avoided, and others (e.g. viral respiratory infections, stress) are difficult to avoid and should be managed when they occur. During the COVID-19 pandemic, many countries have seen a reduction in asthma exacerbations and influenza-related illness, possibly due to handwashing, masks and social/physical distancing, that reduced the incidence of other respiratory infections, including influenza.

TREATMENT IN SPECIFIC POPULATIONS OR CONTEXTS

Pregnancy: asthma control often changes during pregnancy, so asthma should be monitored every 4–6 weeks. For baby and mother, the advantages of actively treating asthma markedly outweigh any potential risks of usual controller and reliever medications. Ensure that all patients are receiving ICS-containing therapy, because asthma exacerbations are associated with increased risk of pre-term delivery, low birth weight and increased perinatal mortality. Down-titration has a low priority in pregnancy, and ICS should not be stopped. Exacerbations should be treated aggressively.

Rhinitis and sinusitis: these often coexist with asthma. Chronic rhinosinusitis and nasal polyposis are associated with more severe asthma. Treatment of allergic rhinitis or chronic rhinosinusitis reduces nasal symptoms but does not improve asthma control.

Obesity: document the diagnosis of asthma in the obese, to avoid over- or under-treatment. Include weight reduction in the treatment plan for obese patients with asthma; even 5–10% weight loss can improve asthma control.

The elderly: comorbidities and their treatment may complicate asthma management. Factors such as arthritis, eyesight, inspiratory flow, and complexity of treatment regimens should be considered when choosing medications and inhaler devices.

Gastroesophageal reflux disease (GERD): this is commonly seen in asthma. Symptomatic reflux should be treated for its general health benefits, but there is no benefit from treating asymptomatic reflux in asthma.

Anxiety and depression: these are commonly seen in people with asthma, and are associated with worse symptoms and quality of life. Patients should be assisted to distinguish between symptoms of anxiety and of asthma.

Aspirin-exacerbated respiratory disease (AERD): a history of exacerbation following ingestion of aspirin or other NSAIDs is highly suggestive. Patients often have severe asthma and nasal polyposis. Confirmation of the diagnosis of AERD may require challenge in a specialized center with resuscitation facilities, but avoidance of NSAIDs may be recommended on the basis of a clear history. ICS are the mainstay of treatment, but OCS may be required; LTRA may also be useful. Desensitization is sometimes effective but must be

done under specialist care; there is a significantly increased risk of adverse effects such as gastritis and gastrointestinal bleeding.

Food allergy and anaphylaxis: food allergy is rarely a trigger for asthma symptoms. It must be assessed with specialist testing. Confirmed food allergy is a risk factor for asthma-related death. Good asthma control is essential; patients should also have an anaphylaxis plan and be trained in appropriate avoidance strategies and use of injectable epinephrine.

Surgery: whenever possible, good asthma control should be achieved pre-operatively. Ensure that controller therapy is maintained throughout the peri-operative period. Patients on long-term high dose ICS, or having more than 2 weeks' OCS in the past 6 months, should receive intra-operative hydrocortisone to reduce the risk of adrenal crisis.

ASTHMA FLARE-UPS (EXACERBATIONS)

A flare-up or exacerbation is an acute or sub-acute worsening in symptoms and lung function from the patient's usual status; occasionally it may be the initial presentation of asthma.

For discussion with patients, the word 'flare-up' is preferred. 'Episodes', 'attacks' and 'acute severe asthma' are often used in medical literature, but they have variable meanings, particularly for patients.

The management of worsening asthma and exacerbations should be considered as a continuum, from self-management by the patient with a written asthma action plan, through to management of more severe symptoms in primary care, the emergency department and in hospital.

Identifying patients at risk of asthma-related death

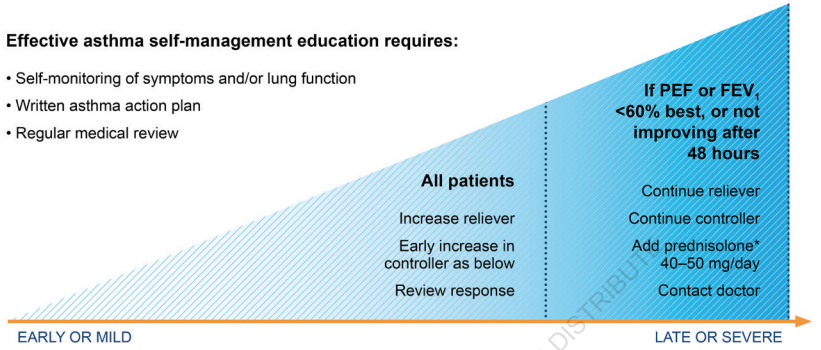
Patients with features indicating increased risk of asthma-related death should be flagged for more frequent review. These features include:

- *History*: A history of near-fatal asthma (ever) requiring intubation and ventilation; hospitalization or emergency care for asthma in the last year
- *Medications*: not currently using ICS, or with poor adherence with ICS; currently using or recently stopped OCS (an indication of recent severity); over-use of SABA, especially if dispensed more than 1 canister (200 doses) per month
- *Comorbidities*: history of psychiatric disease or psychosocial problems; confirmed food allergy in a patient with asthma; comorbidities associated with older age such as pneumonia, diabetes or arrhythmias
- *Lack of a written asthma action plan.*

WRITTEN ASTHMA ACTION PLANS

All patients should be provided with a written asthma action plan appropriate for their level of asthma control and health literacy, so they know how to recognize and respond to worsening asthma.

Box 10. Self-management with a written action plan



The written asthma action plan should include:

- the patient's usual asthma medications
- when and how to increase medications, and start OCS if needed
- how to access medical care if symptoms fail to respond.

Action plans can be based on symptoms and/or (in adults) PEF. Patients who deteriorate quickly should be advised to seek urgent care immediately.

Medication changes for written asthma action plans (for more details about these options, see GINA 2022 full report, Box 4-2)

Increase frequency of inhaled reliever (low dose ICS-formoterol, or SABA); add spacer for pMDI. Advise patients to seek medical care if they are rapidly deteriorating, need SABA reliever again within 3 hours, or need more than 8 BDP-formoterol inhalations or more than 12 budesonide-formoterol inhalations in a day (total 48 mcg and 72 mcg formoterol metered dose respectively). Check local labelling as the maximum total dose may vary.

Increase controller*:* Rapid increase in controller, depending on usual controller medication and regimen, as follows:

- *ICS*: In adults and adolescents, consider quadrupling dose. However, in children with good adherence, a large (5x) increase was not effective.
- *Maintenance ICS-formoterol*: For patients prescribed maintenance and reliever therapy (MART), increase reliever doses of ICS-formoterol as above. For patients prescribed SABA reliever, consider quadrupling maintenance ICS-formoterol dose. Note maximum total formoterol dose above.

- *Maintenance ICS-other LABA*: Step up to higher dose formulation, or consider adding separate ICS inhaler to achieve quadruple ICS dose.
- *Maintenance and reliever ICS-formoterol*: Continue maintenance dose; increase reliever doses as needed (note maximum total dose above).

***Oral corticosteroids** (preferably morning dosing; review before ceasing)*:

- For adults, prednisolone 40–50 mg, usually for 5–7 days.
- For children, prednisolone 1–2 mg/kg/day up to 40 mg, usually for 3–5 days.
- Tapering not needed if OCS has been given for less than 2 weeks.

MANAGING EXACERBATIONS IN PRIMARY OR ACUTE CARE

Assess exacerbation severity while starting SABA and oxygen. Assess dyspnea (e.g. is the patient able to speak sentences, or only words), respiratory rate, pulse rate, oxygen saturation and lung function (e.g. PEF). Check for anaphylaxis.

Consider alternative causes of acute breathlessness (e.g. heart failure, upper airway dysfunction, inhaled foreign body or pulmonary embolism).

Arrange immediate transfer to an acute care facility if there are signs of severe exacerbation, or to intensive care if the patient is drowsy, confused, or has a silent chest. For these patients, immediately give inhaled SABA, inhaled ipratropium bromide, oxygen and systemic corticosteroids.

Start treatment with repeated doses of SABA (usually by pMDI and spacer), early OCS, and controlled flow oxygen if available. Check response of symptoms and saturation frequently, and measure lung function after 1 hour.

Titrate oxygen, if needed, to maintain target saturation of 93–95% in adults and adolescents (94–98% in children 6–12 years).

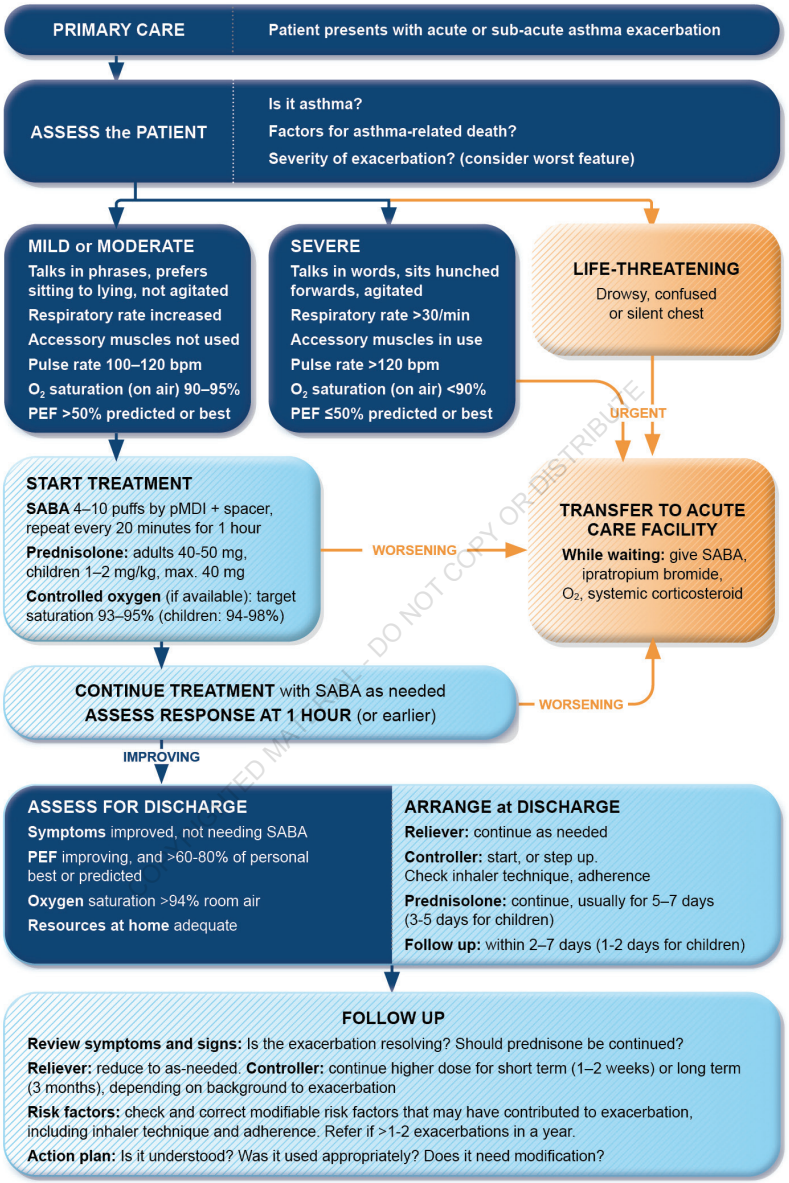
For severe exacerbations, arrange transfer to an acute care facility, add ipratropium bromide, and consider giving SABA by nebulizer (with infection control procedures). In acute care facilities, intravenous magnesium sulfate may be considered for inadequate response to intensive initial treatment.

Do not routinely perform chest X-ray or blood gases, or routinely prescribe antibiotics, for asthma exacerbations.

Box 11 (p.44) summarizes the approach to assessment and management of asthma exacerbations for adults, adolescents and children 6–11 years presenting in primary care.

Currently, inhaled albuterol (salbutamol) is the usual bronchodilator for acute asthma management, but similar efficacy and safety to inhaled albuterol have been reported from several emergency department studies with formoterol and one study with budesonide-formoterol, in patients with FEV_1 >30% predicted.

Box 11. Management of asthma exacerbations in primary care



O_2: oxygen; PEF: peak expiratory flow; SABA: short-acting beta$_2$-agonist (doses are for salbutamol)

REVIEWING RESPONSE

Monitor patients closely and frequently during treatment, and titrate treatment according to response. Transfer to higher level care if worsening or failing to respond. **Decide on need for hospitalization** based on clinical status, symptoms and lung function, response to treatment, recent and history of exacerbations, and ability to manage at home.

Before discharge, arrange ongoing treatment. For most patients, prescribe regular controller therapy (or increase current dose) to reduce the risk of further exacerbations. Continue increased controller doses for 2–4 weeks. Reduce reliever to as-needed dosing, and return patient to as-needed ICS-formoterol reliever if prescribed this before exacerbation. Check inhaler technique and adherence. Provide an interim written asthma action plan.

Arrange early follow-up after any exacerbation, within 2–7 days (for children, within 1–2 working days). Consider early referral for specialist advice after hospitalization, or for patients with repeated ED presentations.

FOLLOW-UP AFTER AN EXACERBATION

Exacerbations often represent failures in chronic asthma care, and they provide opportunities to review the patient's asthma management. **All patients must be followed up regularly by a health care provider until symptoms and lung function return to normal.**

Take the opportunity to review:

- The patient's understanding of the cause of the exacerbation
- Modifiable risk factors for exacerbations, e.g. smoking
- Choice of treatment track – Track 1 (p.22) with ICS-formoterol reliever reduces risk of further severe exacerbations
- Understanding of purposes of medications
- Inhaler technique skills
- Adherence with ICS and OCS as this may fall rapidly after discharge.
- Written asthma action plan – revise if necessary

Comprehensive post-discharge programs that include optimal controller management, inhaler technique, self-monitoring, written asthma action plan and regular review are cost-effective and are associated with significant improvement in asthma outcomes.

Referral for expert advice should be considered for patients who have been hospitalized for asthma, or who re-present for acute asthma care. Patients who have had more than 1 or 2 exacerbations/year despite medium or high dose ICS-LABA should be referred (see GINA 2022 Short guide *Difficult to Treat and Severe Asthma*, www.ginasthma.org/severeasthma/).

GLOSSARY OF ASTHMA MEDICATION CLASSES

For more details about medications, see full GINA 2022 report (www.ginasthma.org) and Product Information from manufacturers. Always check local eligibility criteria.

CONTROLLER MEDICATIONS for MAINTENANCE TREATMENT
Inhaled corticosteroids (ICS)
Medications: Beclometasone, budesonide, ciclesonide, fluticasone propionate, fluticasone furoate, mometasone, triamcinolone. *Devices*: pMDIs or DPIs.
Action and use: ICS-containing medications are the most effective anti-inflammatory medications for asthma. ICS reduce symptoms, increase lung function, reduce airway hyperresponsiveness, improve quality of life, and reduce the risk of exacerbations, asthma-related hospitalizations and death. ICS differ in their potency and bioavailability, but most of the benefit is seen at low doses (see Box 9 (p.30) for low, medium and high doses of different ICS). Adherence with ICS alone (i.e. not in combination inhaler) is usually very poor.
Adverse effects: Most patients do not experience side-effects. Local side-effects include oropharyngeal candidiasis and dysphonia; these can be reduced by use of a spacer with pMDIs, and rinsing with water and spitting out after inhalation. Long-term high doses increase the risk of systemic side-effects such as osteoporosis, cataract and glaucoma.
ICS in combination with a long-acting beta$_2$-agonist bronchodilator (ICS-LABA)
Medications: Beclometasone-formoterol, budesonide-formoterol, fluticasone furoate-vilanterol, fluticasone propionate formoterol, fluticasone propionate-salmeterol, mometasone-formoterol and mometasone-indacaterol. *Devices*: pMDIs or DPIs
Action and use: When a low dose of ICS alone fails to achieve good control of asthma, the addition of LABA to ICS improves symptoms, lung function and reduces exacerbations in more patients, more rapidly, than doubling the dose of ICS. Two regimens are available: low dose combination beclometasone or budesonide with low dose formoterol for maintenance and reliever treatment (MART, GINA Track 1), and maintenance ICS-LABA with SABA as reliever (Track 2). MART with low dose ICS-formoterol reliever is preferred as it reduces exacerbations compared with conventional maintenance therapy with SABA as reliever. (See section on anti-inflammatory relievers below for as-needed ICS-formoterol in mild asthma; and section on add-on controllers for ICS-LABA-LAMA).
Adverse effects: The LABA component may be associated with tachycardia, headache or cramps. LABA is safe for asthma when used in combination with ICS. LABA should not be used without ICS in asthma (or in patients with asthma+COPD) due to increased risk of serious adverse outcomes.
Leukotriene modifiers (leukotriene receptor antagonists, LTRA)
Medications: tablets, e.g. montelukast, pranlukast, zafirlukast, zileuton.
Action and use: Target one part of the inflammatory pathway in asthma. Sometimes used as an option for controller therapy, mainly only in children. When used alone: less effective than low dose ICS. When added to ICS: less effective than ICS-LABA.

Adverse effects: Few in placebo-controlled studies except elevated liver function tests with zileuton and zafirlukast. FDA boxed warning about risk of serious behaviour and mood changes including in children; should be discussed with patients/parents.

ADD-ON CONTROLLER MEDICATIONS for MAINTENANCE TREATMENT

Long-acting muscarinic antagonists (LAMA) (check your local eligibility criteria)

Medications: Tiotropium, ≥6 years, by mist inhaler. For adults ≥18 years: beclometasone-formoterol-glycopyrronium; fluticasone furoate-vilanterol-umeclidinium; mometasone-indacaterol-glycopyrronium. pMDIs or DPIs.

Action and use: An add-on option at Step 5 (or, non-preferred, at Step 4) for patients with uncontrolled asthma despite ICS-LABA. Modestly improves lung function but not symptoms or quality of life; small reduction in exacerbations. For patients with exacerbations, ensure that ICS is increased to at least medium dose before considering need for add-on LAMA.

Adverse effects: Uncommon, but include dry mouth, urinary retention.

Anti-IgE (check your local eligibility criteria)

Medications: Omalizumab, ≥6 years, subcutaneous (SC) injection

Action and use: An add-on option for patients with severe allergic asthma uncontrolled on high dose ICS-LABA. May also be indicated for nasal polyposis and chronic idiopathic urticaria. Self-administration may be an option.

Adverse effects: Reactions at the site of injection are common but minor. Anaphylaxis is rare.

Anti-IL5 and anti-IL5R (check your local eligibility criteria)

Medications: Anti-IL5: mepolizumab (≥12 years, SC injection) or reslizumab (≥18 years, intravenous injection). Anti-IL5 receptor benralizumab (≥12 years, SC injection).

Action and use: Add-on options for patients with severe eosinophilic asthma uncontrolled on high dose ICS-LABA. Maintenance OCS dose can be significantly reduced with benralizumab and mepolizumab. Mepolizumab may also be indicated for eosinophilic granulomatosis with polyangiitis (EGPA), hypereosinophilic syndrome or chronic rhinosinusitis with nasal polyposis. For mepolizumab and benralizumab, self-administration may be an option

Adverse effects: Headache, and reactions at injection site are common but minor.

Anti-IL4R (check your local eligibility criteria)

Medications: Anti-interleukin 4 receptor alpha: dupilumab, ≥6 years, SC injection

Action and use: An add-on option for patients with severe eosinophilic or Type 2 asthma uncontrolled on high dose ICS-LABA, or requiring maintenance OCS. Not advised for patients with blood eosinophils ≥1500/μl. May also be indicated for treatment of moderate-severe atopic dermatitis and chronic rhinosinusitis with nasal polyposis. Self-administration may be an option.

Adverse effects: Reactions at injection site are common but minor. Blood eosinophilia occurs in 4–13% of patients. Rarely, cases of eosinophilic granulomatosis with polyangiitis (EGPA) may occur.

Anti-TSLP (check your local eligibility criteria)

Medications: Tezepelumab, SC injection, ≥12 years

Action and use: An add-on option for patients with severe asthma uncontrolled on high dose ICS-LABA. In patients taking maintenance OCS, no significant reduction in OCS dose.

Adverse effects: Injection-site reactions; anaphylaxis is rare; adverse events generally similar between active and placebo groups.

Systemic corticosteroids

Medications: include prednisone, prednisolone, methylprednisolone, hydrocortisone tablets, dexamethasone. Given by tablets or suspension or by IM or IV injection

Action and use: Short-term treatment (usually 5–7 days in adults) is important in the treatment of severe acute exacerbations, with main effects seen after 4–6 hours. For exacerbations, OCS therapy is preferred to IM or IV therapy and is effective in preventing relapse. Tapering is required if treatment given for more than 2 weeks. As a last resort, long-term treatment with OCS may be required for some patients with severe asthma, but side-effects are problematic.

Adverse effects: Short courses: adverse effects include sepsis, thromboembolism, sleep disturbance, reflux, appetite increase, hyperglycemia, mood changes. Even 4–5 lifetime courses increase cumulative risk of long-term adverse effects e.g. diabetes, osteoporosis, cataract, glaucoma, heart failure.

Maintenance use: consider only as last resort, because of significant adverse effects e.g. cataract, glaucoma, hypertension, diabetes, adrenal suppression osteoporosis. Assess for these risks and treat appropriately.

ANTI-INFLAMMATORY RELIEVER MEDICATIONS

Low dose ICS-formoterol

Medications: Beclometasone-formoterol or budesonide-formoterol. pMDIs or DPIs

Action and use: This is the reliever inhaler for patients with moderate-severe asthma prescribed maintenance and reliever therapy (MART) with ICS-formoterol, or for patients with mild asthma prescribed as-needed ICS-formoterol alone. In both settings, it reduces the risk of severe exacerbations compared with using SABA as reliever, with similar symptom control. In patients with mild asthma, as-needed ICS-formoterol reduces emergency visits/hospitalisations compared with daily ICS plus as-needed SABA. Reduces exercise-induced bronchoconstriction when taken before exercise.

Adverse effects: As for ICS-formoterol above. The maximum total dose recommended in a single day (maintenance plus reliever doses) for BDP-formoterol is 48 mcg formoterol (36 mcg delivered dose), and for budesonide-formoterol, 72 mcg formoterol (54 mcg delivered dose).

SHORT-ACTING BRONCHODILATOR RELIEVER MEDICATIONS

Short-acting inhaled beta$_2$-agonist bronchodilators (SABA)

Medications: e.g. salbutamol (albuterol), terbutaline. Administered by pMDIs, DPIs and, rarely, as solution for nebulization or injection

Action and use: Inhaled SABAs provide quick relief of asthma symptoms and bronchoconstriction, and for pre-treatment of exercise-induced bronchoconstriction. SABAs should be used only as-needed (not regularly) and at the lowest dose and frequency required. SABA-only treatment is not recommended because of the risk of severe exacerbations and asthma-related death. Currently, inhaled SABAs are the usual bronchodilator for acute exacerbations requiring urgent primary care visit or ED presentation.
Adverse effects: Tremor and tachycardia are commonly reported with initial use of SABA. Tolerance develops rapidly with even 1–2 weeks of regular use, with increased airway hyperresponsiveness, reduced bronchodilator effect, and increased airway inflammation. Excess use, or poor response indicate poor asthma control and risk of exacerbations. Dispensing of ≥3x200-dose canisters per year is associated with increased risk of exacerbations; dispensing of ≥12 canisters per year associated with markedly increased risk of death.
Short-acting anticholinergics
Medications: e.g. ipratropium bromide, oxitropium bromide. May be in combination with SABAs. pMDIs or DPIs.
Action and use: Long-term use: ipratropium is a less effective reliever medication than SABAs. Short-term use in severe acute asthma: adding ipratropium to SABA reduces the risk of hospital admission
Adverse effects: Dryness of the mouth or a bitter taste.

ACKNOWLEDGEMENTS

The activities of the Global Initiative of Asthma are supported by the work of members of the GINA Board of Directors and Committees (listed below), and by the sale of GINA products. The members of the GINA committees are solely responsible for the statements and recommendations presented in this and other GINA publications.

GINA Science Committee (2021–2022)

Helen Reddel, Australia, *Chair*; Leonard Bacharier, USA; Eric Bateman, South Africa.; Louis-Philippe Boulet*, Canada; Christopher Brightling, UK; Guy Brusselle, Belgium; Roland Buhl, Germany; Liesbeth Duijts, The Netherlands; Jeffrey Drazen, USA; J. Mark FitzGerald, Canada (deceased); Louise Fleming, UK; Hiromasa Inoue*, Japan; Fanny Wai-san Ko, Hong Kong; Jerry Krishnan*, USA; Kevin Mortimer, UK; Paulo Pitrez, Brazil; Aziz Sheikh, UK.

GINA Board of Directors (2021–2022)

Louis-Philippe Boulet*, Canada, *Chair;* Eric Bateman, South Africa; Guy Brusselle, Belgium; Alvaro Cruz*, Brazil; J Mark FitzGerald, Canada (deceased); Hiromasa Inoue*, Japan; Jerry Krishnan, USA; Mark Levy*, United Kingdom; Jiangtao Lin, China (to 2021); Helen Reddel, Australia; Arzu Yorgancioglu*, Turkey.

GINA Dissemination and Implementation Committee (2021–2022)

Mark Levy, UK, *Chair*; other members indicated by asterisks (*) above.

GINA Advocates and Assembly

Representatives are from multiple countries. Names are listed on the GINA website.

GINA Program: Executive Director: Rebecca Decker, USA, Program Director: Kristi Rurey, USA

Editorial assistance: Jenni Harman, Ruth Hadfield

ADDITIONAL GINA RESOURCES

- **Global Strategy for Asthma Management and Prevention** (updated 2022). This report provides an integrated approach to asthma that can be adapted for a wide range of health systems. The report has a user-friendly format with many practical summary tables and flow-charts for use in clinical practice. It is updated yearly.
- **GINA Online Appendix** (updated 2022). Detailed information to support the main GINA report. Updated yearly.
- **Difficult-to-treat and severe asthma in adolescent and adult patients. Diagnosis and Management. A short GINA Guide for Health Professionals V4.0, 2022.** This short guide includes a decision tree about how to assess and manage patients presenting with uncontrolled asthma despite medium or high dose ICS-LABA. Content of this guide is included in the full GINA 2022 report.
- **A toolbox of clinical practice aids and implementation tools**
- **COVID-19 and asthma:** This slide set provides practical advice about asthma and COVID-19. It is updated as new information is available.

GINA publications and other resources are available from www.ginasthma.org

Visit the GINA website at
www.ginasthma.org