

stepwise treatment of asthma



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Definition



- ❑ The stepwise approach to the pharmacologic treatment of asthma is a core foundation of asthma guidelines
- ❑ The stepwise approach to therapy, in which **the dose and number of medications and frequency of administration are increased as necessary and decreased when possible**, is used to achieve and maintain this control.
- ❑ Through this approach, treatment intensity is increased in discrete steps to obtain symptom control and reduce exacerbation risk and is decreased after a period of prolonged control.
- ❑ The antiinflammatory reliever–based algorithm using ICS/formoterol can be based on four steps, the first step being use of ICS/formoterol as the sole reliever therapy

Definition



- Asthma is a disease with many variations (phenotypes), usually characterized by chronic airway inflammation.
- Assessment of a patient with asthma includes not only symptom control, but also the patient's individual risk factors and comorbidities.

Asthma control – assess both symptom control and risk factors



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

Watch patient using their inhaler. Discuss adherence and barriers to use

Compare inhaler technique with a device-specific checklist, and correct errors; recheck frequently. Have an empathic discussion about barriers to adherence.

Confirm the diagnosis of asthma

If lung function normal during symptoms, consider halving ICS dose and repeating lung function after 2–3 weeks.

Remove potential risk factors. Assess and manage comorbidities

Check for risk factors or inducers such as smoking, beta-blockers, NSAIDs, allergen exposure. Check for comorbidities such as rhinitis, obesity, GERD, depression/anxiety.

Consider treatment step-up

Consider step up to next treatment level. Use shared decision-making, and balance potential benefits and risks.

Refer to a specialist or severe asthma clinic

If asthma still uncontrolled after 3–6 months on Step 4 treatment, refer for expert advice. Refer earlier if asthma symptoms severe, or doubts about diagnosis.



How to investigate uncontrolled asthma in primary care

GOALS OF ASTHMA TREATMENT

□ Optimizing control of asthma symptoms:

- Good control of asthma means reducing the intensity and frequency of asthma symptoms

(reducing cough, chest tightness, wheezing, or shortness of breath)

- maintaining normal or near normal activity levels (including work or school attendance and participation in athletics and exercise)

❑ Reducing future risk:

exacerbations,

- suboptimal lung development (children), loss of lung function over time (adults),
- adverse effects from asthma medications

❑ Risk factor for exacerbat

- A history of ≥ 1 exacerbation(s) in the past year ,ever intubatioor ICU care
- poor adherence to asthma medication,
- incorrect inhaler technique,
- low lung function($FEV1 < 60\%$, higher revsibility)
- smoking (eg, tobacco, cannabis) or vaping,
- an elevated concentration FeNO
- blood eosinophilia

Cont ...



□ Specific goals:

- Prevention of recurrent exacerbations
- Prevention of reduced lung growth in children and loss of lung function in adults
- Optimization of pharmacotherapy with minimal or no adverse effects

ADJUSTING CONTROLLER MEDICATION



- ☐ Therapy should be reassessed at each visit (over the past two to four weeks with history or a validated questionnaire, FEV1 or PEF)
- ☐ 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.
- ☐ In patients with poorly controlled asthma, treatment should be "stepped up.
- ☐ In patients with very poorly controlled asthma, it may be necessary to escalate therapy more than one step, and then "stepdown" again once good control is achieved.

Treatment can be stepped up or down with using the same reliever at each step, according to the individual patient's needs.



STEP 1.

Preferred treatment for adults and adolescents: low dose ICS-formoterol taken as needed for symptom relief.

1- Initial asthma treatment for patients with symptoms less than twice a month and no exacerbation risk factors, a group that is rarely studied

2- Step-down treatment for patients whose asthma is well-controlled on Step 2 treatment

Regular use of SABA for 1–2 weeks leads to increased airway hyperresponsiveness and reduced bronchodilatation

SABA over-use (e.g. dispensing of $>3 \times 200$ -dose canisters/year) is associated with increased risk of exacerbations and death.



Low dose ICS taken whenever SABA is taken:

This may be an option if as-needed ICS-formoterol is not available

The usual dose of as-needed budesonide-formoterol in mild asthma is one inhalation of 200/6 mcg (delivered dose 160/4.5) 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).

STEP 2.



1-Preferred treatment for adults and adolescents: low dose ICS-formoterol taken as needed for symptom relief

❖ Severe exacerbations are halved even in patients with symptoms 0–1 days a week.

2- daily low dose ICS plus as-needed SABA

3-Low dose ICS taken whenever SABA is taken

4-Leukotriene receptor antagonists (LTRA) are less effective than regular ICS, particularly for preventing exacerbations.

STEP 3.



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

- ❑ ***Preferred treatment for adults and adolescents:***
 - ❖ ***low dose ICS-formoterol maintenance and reliever therapy***
 - ❖ as both maintenance and reliever treatment (MART).

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 72mcg formoterol for budesonide-formoterol (54 mcg delivered dose).

BDP:Beclometasone dipropionate

Other controller options for adults and adolescents:

Medium dose ICS, or low dose ICS plus LTRA.

For adult patients with rhinitis who are allergic to house dust mite, consider adding sublingual immunotherapy (SLIT), ***provided FEV1 is >70% predicted***

STEP 4.



❖ Preferred treatment for adults and adolescents:

- *Medium dose ICS-formoterol as maintenance and reliever therapy*
- patients whose asthma is uncontrolled on Step 3 treatment despite good adherence and correct technique may benefit from increasing the maintenance ICS dose to medium.

• Alternative Step 4

Some patients whose asthma is uncontrolled or who have frequent exacerbations on low dose ICS-LABA ,recommended **medium or high dose ICS-LABA with as-needed SABA**

- include add-on LAMA for patients ≥ 18 years (≥ 6 years for tiotropium by mist haler) in separate or combination ('triple') inhalers.
- Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium, or switch to maintenance and reliever therapy.

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- ❑ In treating severe asthma add:
 - a long-acting muscarinic antagonist (LAMA; eg, tiotropium) and/or a
 - leukotriene modifier to the combination ICS/LABA.

- ❑ When severe asthma remains poorly controlled, oral glucocorticoids may be needed on a daily or alternate-day basis.

- ❑ For patients whose asthma is inadequately controlled on medium- to high-dose inhaled glucocorticoids and LABAs,
 - The anti-IgE therapy **omalizumab** may be considered if there is objective evidence of sensitivity to a perennial allergen (by allergy skin tests or in vitro measurements of allergen-specific IgE) and if the serum total IgE level is within the established target range (based on patient weight and serum total IgE level).

STEP 5.

Refer for phenotypic investigation ± add-on treatment

- 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,
- and anti-IL5 (SC mepolizumab, ≥ 6 years, or IV reslizumab, ≥ 18 years) or
- anti-IL5R (SC benralizumab, ≥ 12 years) or
- anti-IL4R (SC dupilumab, ≥ 12 years) for severe eosinophilic asthma.

Add-on azithromycin three days/week reduces exacerbations, but antibiotic resistance increases.



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

Stepping up asthma treatment



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:

- o incorrect inhaler technique
- o poor adherence
- o modifiable risk factors, e.g. smoking
- o 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 e.g. during viral infection or allergen exposure

- *Day-to-day adjustment by patient* with as-needed low dose ICS-formoterol for mild asthma, or ICS-formoterol as maintenance and reliever therapy. This is particularly effective in reducing severe exacerbations .

Stepping down treatment when asthma is well-controlled



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), and follow-up visit
- Step down through available formulations to reduce the ICS dose by 25–50% at 2–3 month intervals (see Box 3-9 in full GINA 2021 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)
- 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.

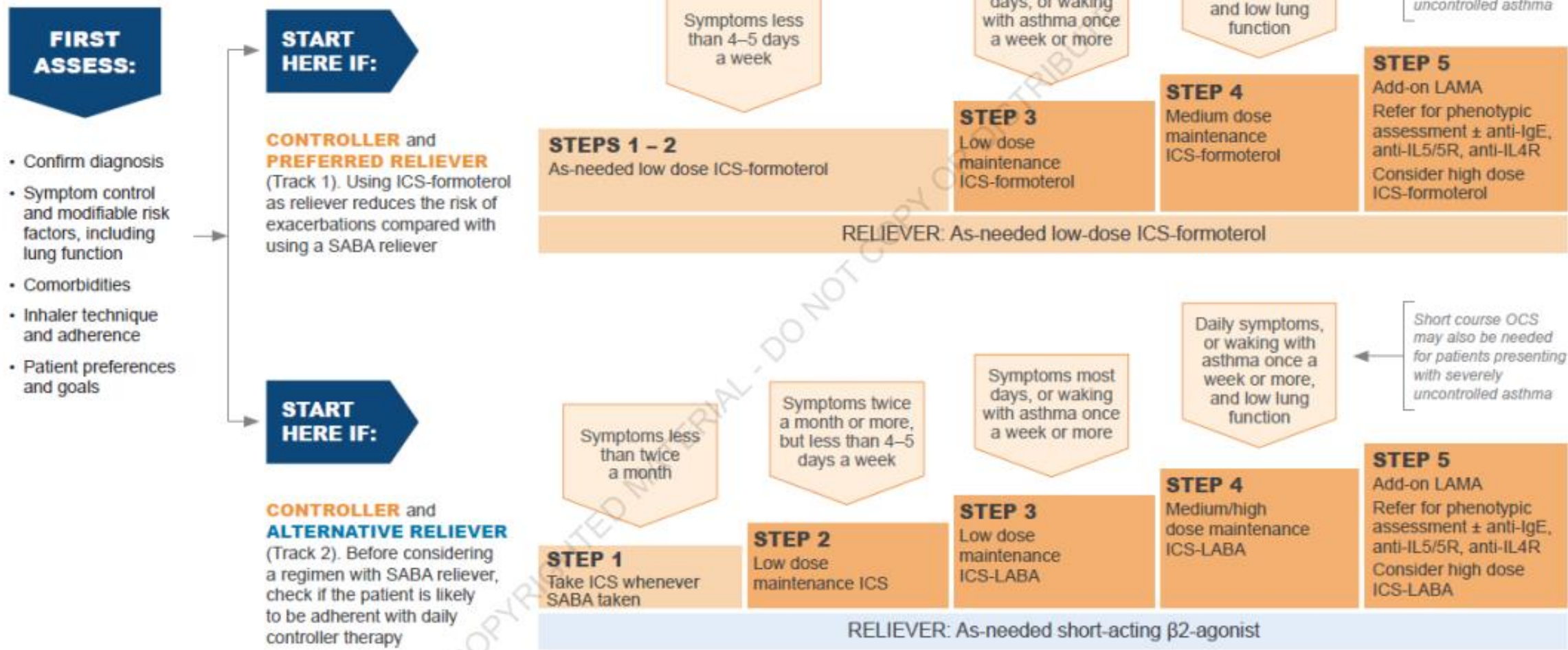
STARTING TREATMENT

in adults and adolescents with a diagnosis of asthma

Track 1 is preferred if the patient is likely to be poorly adherent with daily controller ICS-containing therapy is recommended even if symptoms are infrequent, as it reduces the risk of severe exacerbations and need for OCS.



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ICS: inhaled corticosteroid; SABA: short-acting beta₂-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 2021 report (www.ginasthma.org). For more details about Step 5 add-on therapies, see Chapter 3E of the GINA report, or the GINA 2021 Pocket Guide on Difficult to Treat and Severe Asthma, and check eligibility criteria with local payers.

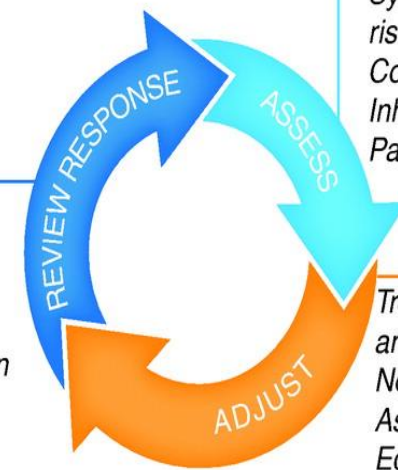
Personalized management for adults and adolescents to control symptoms and minimize future risk. The 2020 Global Initiative for Asthma algorithm.
Am J Respir Crit Care Med, 2021
<https://www.atsjournals.org/doi/abs/10.1164/rccm.202101-0224LE>

Adults & adolescents 12+ years

Personalized asthma management:

Assess, Adjust, Review response

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down or up)
Education & skills training

Asthma medication options:

Adjust treatment up and down for individual patient needs

PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

Other controller options

PREFERRED RELIEVER

Other reliever options

STEP 1		STEP 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol*	As-needed low dose ICS-formoterol*	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol*	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA
	Low dose ICS taken whenever SABA is taken †	Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken †	Medium dose ICS, or low dose ICS+LTRA#	High dose ICS, add-on tiotropium, or add-on LTRA#	Refer for phenotypic assessment ± add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
As-needed low dose ICS-formoterol*		As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy‡			
		As-needed short-acting β_2 -agonist (SABA)			
		Add low dose OCS, but consider side-effects			

* Data only with budesonide-formoterol (bud-form)
† Separate or combination ICS and SABA inhalers

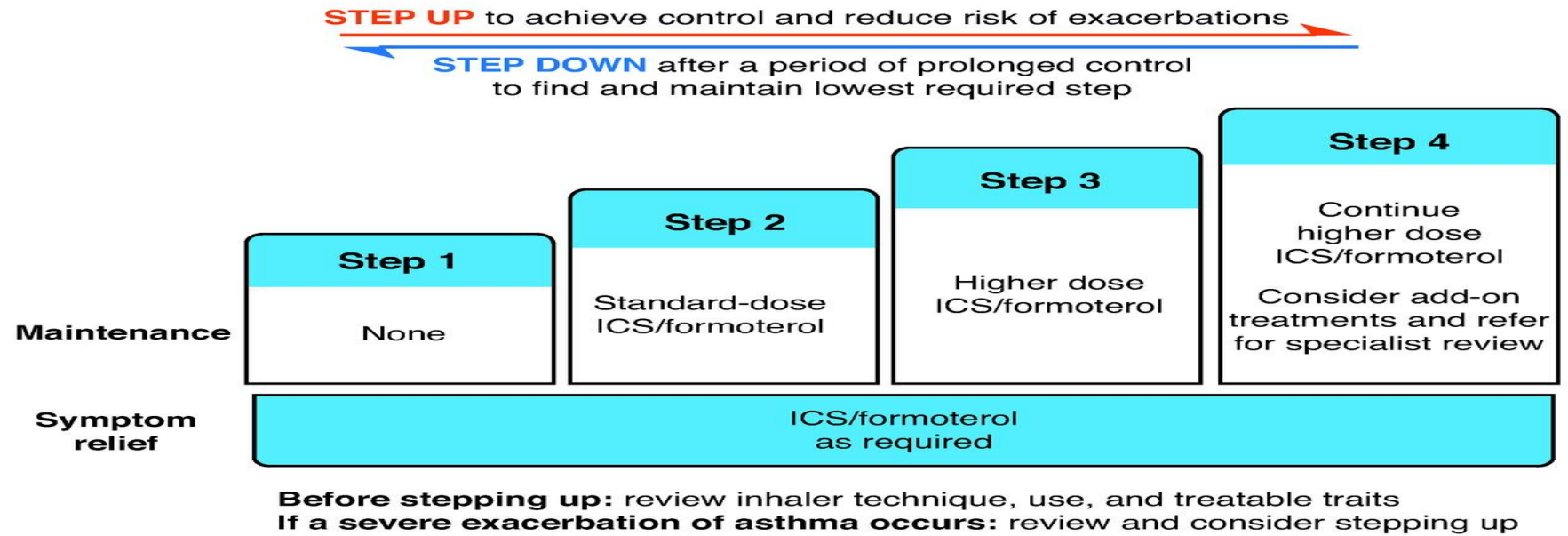
‡ Low-dose ICS-form is the reliever only for patients prescribed bud-form or BDP-form maintenance and reliever therapy
Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 > 70% predicted



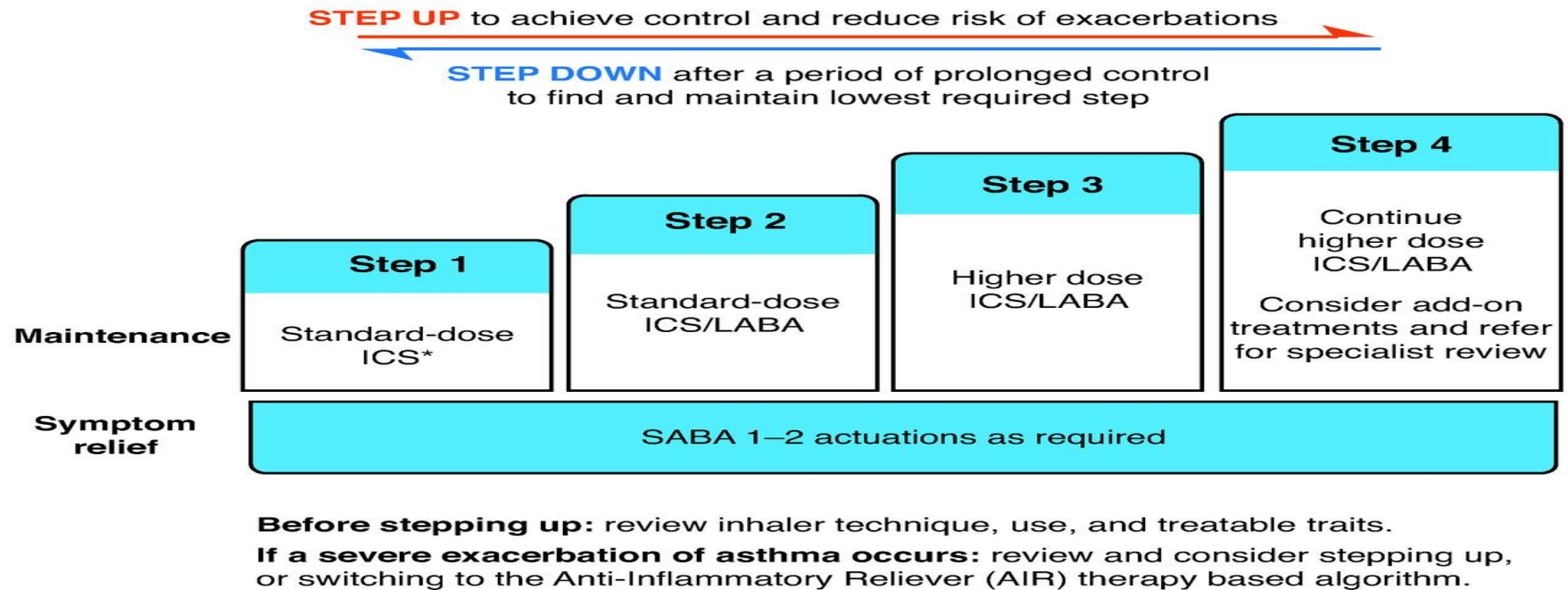
The prototypic algorithms based on (A) antiinflammatory reliever therapy and (B) SABA reliever therapy. *Or standard-dose ICS taken whenever SABA is taken.

Am J Respir Crit Care Med, 2021

A Anti-inflammatory Reliever therapy (AIR) based algorithm using ICS/formoterol



B Traditional SABA reliever therapy based algorithm for asthma management



Adults and adolescents
Inhaled corticosteroid

Total daily ICS dose (mcg)

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

recommended for step 1:

The traditional SABA reliever–based algorithm can also comprise four steps . With the recommendation that a SABA should no longer be used as the sole reliever therapy without an ICS ,regularly scheduled maintenance ICS therapy together with SABA reliever therapy (currently one of the preferred treatment options at GINA step 2).

At steps 2 and 3/4:

“standard”-dose (low-dose) and “higher”-dose (medium- or high-dose) maintenance ICS/LABA and SABA reliever therapies are recommended.

steps 3 and 4/5:

the add-on therapies in severe asthma are introduced at step 4 (previously GINA step 5).

