Asthma

What is new in treatment

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Fars Pediatric Association

Global Initiative for Asthma (GINA)

What's new in GINA?

GINA Global Strategy for Asthma Management and Prevention

World Asthma Day
• May 7, 2024 •

ginasthma.org | @ginasthma

ASTHMA EDUCATION EMPOWERS

Information is Key

Asthma remains the most common chronic illness in children and adolescents globally in world

Goals of asthma treatment

- Few asthma symptoms
- No sleep disturbance
- No exercise limitation

} Symptom control (e.g. ACT, ACQ)

- Maintain normal lung function
- Prevent flare-ups (exacerbations)
- Prevent asthma deaths
- Minimize medication side-effects (including OCS)

} Risk reduction

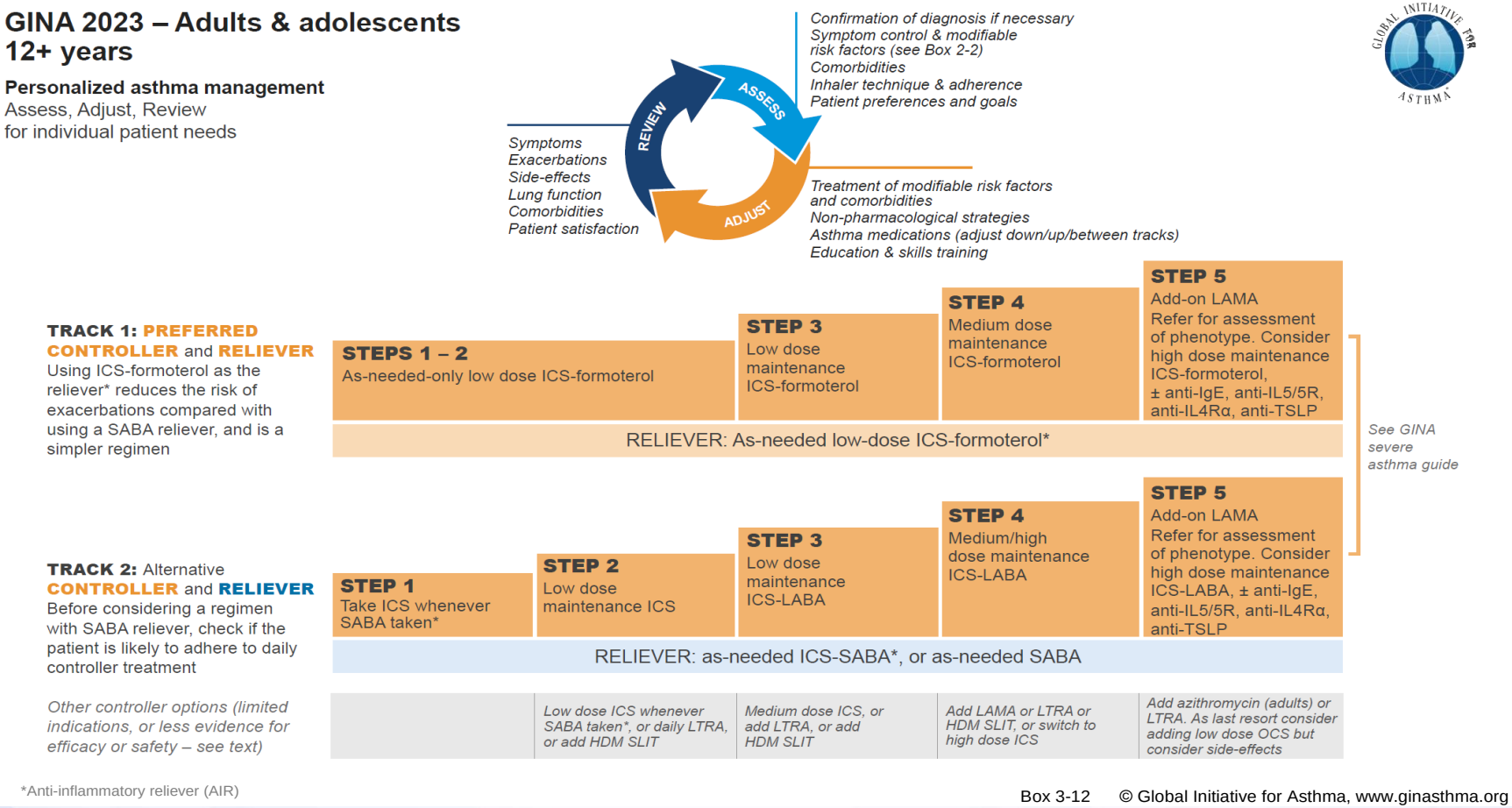
- The patient's goals may be different
- Symptom control and risk may be discordant
  - Patients with few symptoms can still have severe exacerbations

ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; OCS: oral corticosteroids

FIGURE 3–4c. CLASSIFYING ASTHMA SEVERITY IN YOUTHS ≥12 YEARS OF AGE AND ADULTS

- **Classifying severity for patients who are not currently taking long-term control medications.**

Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20–39 yr 80% 40–59 yr 75% 60–80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1			

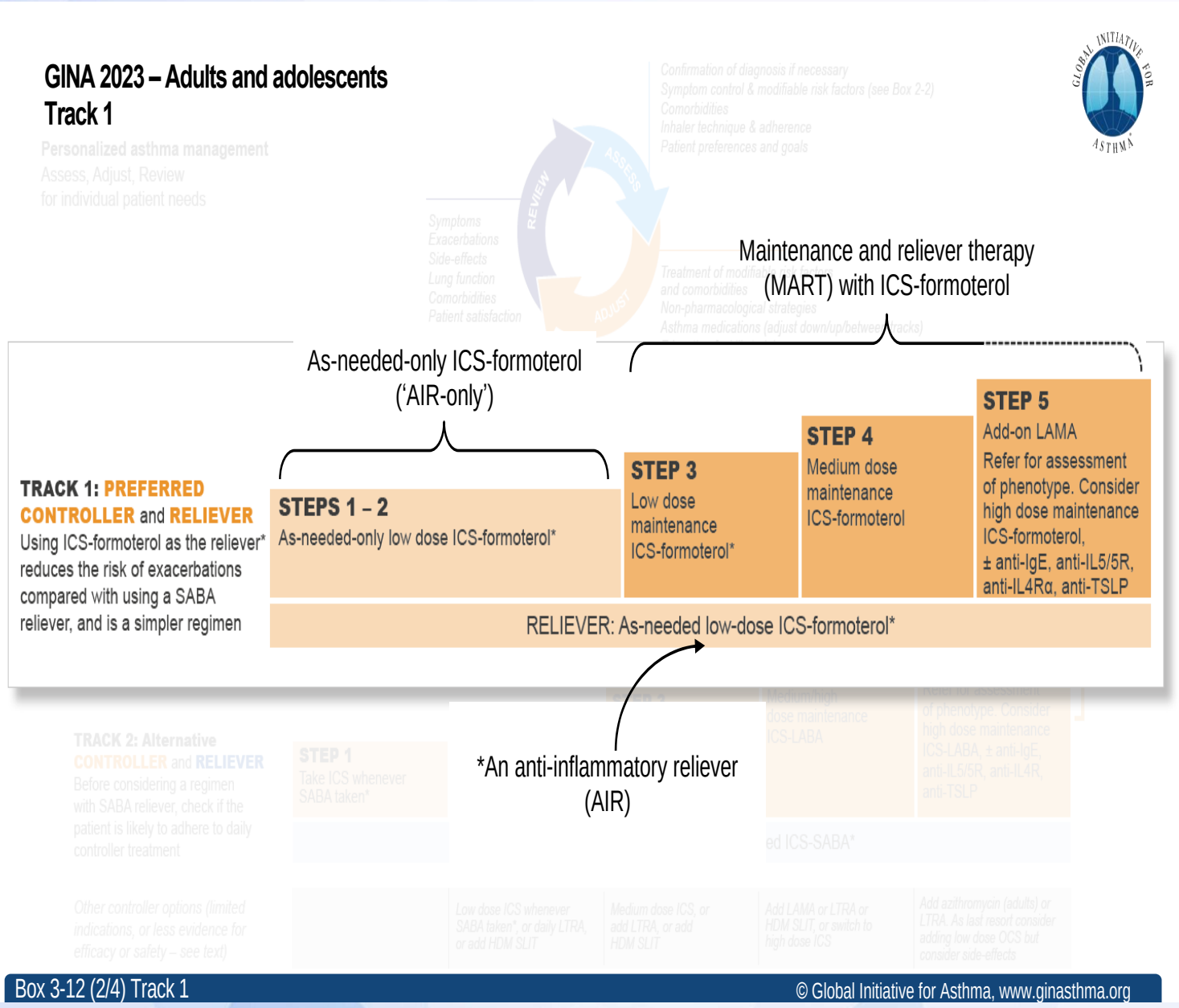


Box 3-12

SPEAKERS: Changes in GINA 2023 for adults and adolescents :

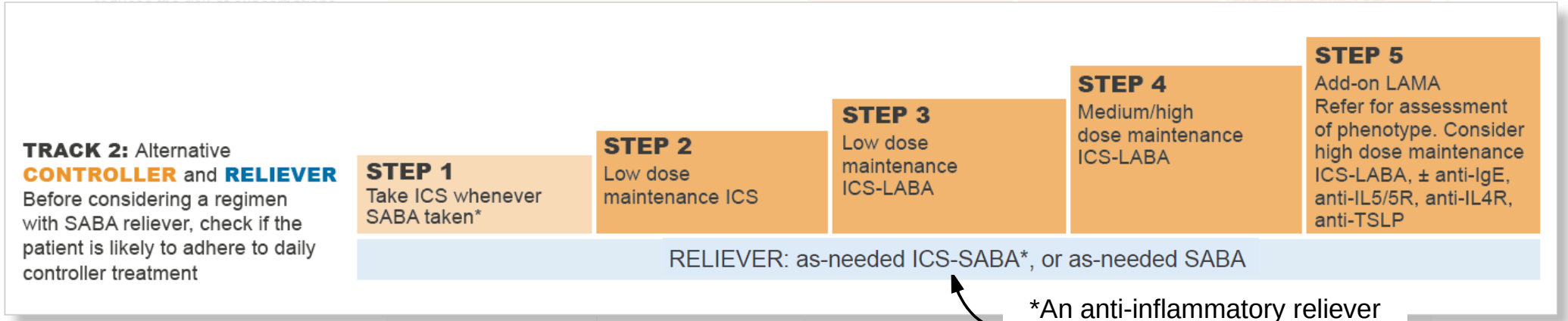
1. Year added at top left, to avoid use of out-of-date versions of GINA figures
2. Rationale for Track 1 being the preferred regimen has been updated (see details on later slides)
3. As-needed ICS-SABA (if available) has been added as a reliever option in Track 2 for Steps 3–5, with most of the benefit seen in Step 3
4. Anti-inflammatory relievers have been identified with an asterisk (see next 2 slides for details)

NOTE: in Step 5, 'add-on LAMA' can be combination (triple) or separate inhalers. If a patient is prescribed triple therapy with a non-formoterol LABA, the reliever should be SABA or ICS-SABA (not ICS-formoterol).



1. MART was originally called SMART, with the 'S' coming from the brandname of the medication used in most of the studies. The 'S' can now stand for 'single inhaler', but this may cause confusion because patients may have two ICS-formoterol inhalers, one at home for their maintenance treatment, and one in their bag/pocket for as-needed doses when they are away from home.
2. Step 5: The dotted line for MART is to indicate that there is no evidence, in a patient taking Step 5 treatment, for switching from a SABA reliever to an ICS-formoterol reliever. However, if a patient already prescribed MART is stepped up from Step 4 to Step 5, e.g. with addition of biologic therapy, there is no need to swjtch their reliever from ICS-formoterol to SABA.
3. In Step 5, 'add-on LAMA' can be combination (triple) or separate inhalers. If a patient is prescribed triple therapy with a non-formoterol LABA, the reliever should be SABA or ICS-SABA (not ICS-formoterol).

GINA 2023 – Adults and adolescents
Track 2



Box 3-12 (3/4) Track 2

GINA 2023 – Adults and adolescents

12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

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

Other controller options (limited indications, or less evidence for efficacy or safety – see text)		*Low dose ICS whenever SABA taken*, or daily LTRA, or add HDM SLIT*	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

TRACK 2: Alternative **CONTROLLER** and **RELIEVER**
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: as-needed SABA, or as-needed ICS-SABA*

Other controller options (limited indications, or less evidence for efficacy or safety – see text)
Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT*
Medium dose ICS, or add LTRA, or add HDM SLIT
Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS
Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects

Box 3-12 4/4)

Terminology

- **A**nti-**I**nflammatory **R**eliever = **AIR**
  - e.g. ICS-formoterol, ICS-SABA
  - Provides rapid symptom relief, plus a small dose of ICS
  - Reduces the risk of exacerbations, compared with using a SABA reliever

Regimens with ICS-formoterol anti-inflammatory reliever

- As-needed-only ICS-formoterol = **AIR-only**
  - The patient takes low-dose ICS-formoterol whenever needed for symptom relief
- **M**aintenance **A**nd **R**eliever **T**herapy with ICS-formoterol = **MART**
  - A low dose of ICS-formoterol is used as the patient's maintenance treatment, plus whenever needed for symptom relief
- ICS-formoterol can also be used before exercise or allergen exposure

ICS: inhaled corticosteroid: SABA: short-acting beta$_2$-agonist; MART is sometimes also called SMART

GINA 2019 – landmark changes in asthma management

- For safety, GINA no longer recommends SABA-only treatment for Step 1
  - This decision was based on evidence that SABA-only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk

- GINA now recommends that all adults and adolescents with asthma should receive
  ICS-containing controller treatment, to reduce the risk of serious exacerbations
  - The ICS can be delivered by regular daily treatment or, in mild asthma, by as-needed low dose ICS-formoterol

- Key changes in GINA 2021 include division of the treatment figure for adults and adolescents into two tracks.
  - Track 1 (preferred) has low-dose ICS-formoterol as the reliever at all steps: as needed only in Steps 1-2 (mild asthma), and with daily maintenance ICS-formoterol (maintenance-and-reliever therapy, “MART”) in Steps 3-5.
  - Track 2 (alternative) has as-needed SABA across all steps, plus regular ICS (Step 2) or ICS-long-acting b2-agonist (Steps 3-5).

How to prescribe low-dose ICS-formoterol in GINA Track 1

Example: budesonide-formoterol 200/6 mcg [160/4.5 delivered dose]

- **Steps 1–2**: take 1 inhalation whenever needed for symptoms
- **Step 3**: take 1 inhalation twice a day (or once a day) PLUS 1 inhalation whenever needed for symptoms
- **Steps 4–5**: take 2 inhalations twice a day PLUS 1 inhalation whenever needed for symptoms
- As-needed doses of ICS-formoterol can also be taken before exercise *(Lazarinis et al, Thorax 2014)* or before allergen exposure *(Duong et al, JACI 2007)*

See following slides for medications, doses, and maximum number of inhalations in any day for GINA Track 1

Reliever doses of ICS-formoterol - how much can be taken?

- For ICS-formoterol with 6 mcg (4.5 mcg delivered dose) of formoterol, take **1 inhalation** whenever needed for symptom relief
- Another inhalation can be taken after a few minutes if needed
- Maximum total number of inhalations in any single day (as-needed + maintenance)
  - **Budesonide-formoterol**: maximum 12 inhalations* for adults, 8 inhalations for children, based on extensive safety data *(Tattersfield et al, Lancet 2001; Pauwels et al, ERJ 2003)*
  - **Beclometasone-formoterol**: maximum total 8 inhalations in any day *(Papi et al, Lancet Respir Med 2013)*
- Emphasize that most patients need far fewer doses than this!
- For pMDIs containing 3 mcg formoterol (2.25 mcg delivered dose), take 2 inhalations each time

**For budesonide-formoterol 200/6 [delivered dose 160/4.5 mcg], 12 inhalations gives 72 mcg formoterol (54 mcg delivered dose)*

Action plan for MART with ICS-formoterol

A Practical Guide to Implementing SMART in Asthma Management

Helen K. Reddel, MB, BS, PhD[a,*], Eric D. Bateman, MB, ChB, MD[b,*], Michael Schatz, MD, MS[c], Jerry A. Krishnan, MD, PhD[d], and Michelle M. Cloutier, MD[e] *Sydney, Australia; Cape Town, South Africa; Chicago, Ill; and Farmington, Conn*

Reddel et al, JACI in Practice 2022; 10: S31-s38

This article includes a writable action plan template
That can be modified for other combination ICS-formoterol inhalers, and for as-needed-only ICS-formoterol

For additional action plans with ICS-formoterol reliever, see National Asthma Council Australia Action plan library
www.nationalasthma.org.au/health-professionals/asthma-action-plans

My Asthma Action Plan

For Single Inhaler Maintenance and Reliever Therapy (SMART)
with budesonide/formoterol

Name: _____ Action plan provided by: _____

Date: _____ Doctor: _____

Usual best PEF: _____ L/min *(if used)* Doctor's phone: _____

Normal mode

My SMART Asthma Treatment is:
- ☐ budesonide/formoterol 160/4.5 (12 years or older)
- ☐ budesonide/formoterol 80/4.5 (4-11 years)

My Regular Treatment Every Day:

(Write in or circle the number of doses prescribed for this patient)

Take [1, 2] inhalation(s) in the morning

and [0, 1, 2] inhalation(s) in the evening, every day

Reliever

Use 1 inhalation of budesonide/formoterol whenever needed for relief of my asthma symptoms

I should always carry my budesonide/formoterol inhaler

My asthma is stable if:
- I can take part in normal physical activity without asthma symptoms

AND
- I do not wake up at night or in the morning because of asthma

Other Instructions

_____

_____

Asthma Flare-up

If over a Period of 2-3 Days:
- My asthma symptoms are getting worse **OR NOT** improving

OR
- I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years or older) or more than 4 inhalations a day (if aged 4-11 years)

I should:

☒ Continue to use my regular everyday treatment **PLUS** 1 inhalation budesonide/formoterol whenever needed to relieve symptoms

☐ Start a course of prednisolone

☐ Contact my doctor

Course of Prednisolone Tablets:

Take _____mg prednisolone tablets per day for _____days **OR**

_____

_____

If I need more than **12 budesonide/formoterol inhalations (total)** in any day (or more than 8 inhalations for children 4-11 years), I **MUST** see my doctor or go to the hospital the same day.

Asthma Emergency

Signs of an Asthma Emergency:
- Symptoms getting worse quickly
- Extreme difficulty breathing or speaking
- Little or no improvement from my budesonide/formoterol reliever inhalations

If I have any of the above danger signs, I should dial _____ for an ambulance and say I am having a severe asthma attack.

While I am waiting for the ambulance start my asthma first aid plan:
- Sit upright and stay calm.
- Take 1 inhalation of budesonide/formoterol. Wait 1-3 minutes. If there is no improvement, take another inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion).
- If only albuterol is available, take 4 puffs as often as needed until help arrives.
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance.
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack.

Modified from Australian action plan with permission from National Asthma Council Australia and AstraZeneca Australia

My Asthma Action Plan

For Single Inhaler Maintenance and Reliever Therapy (SMART)
with budesonide/formoterol

Name: _____ **Action plan provided by:** _____

Date: _____ **Doctor:** _____

Usual best PEF: _____ L/min *(if used)* **Doctor's phone:** _____

Normal mode

My SMART Asthma Treatment is:

☐ budesonide/formoterol 160/4.5 (12 years or older)

☐ budesonide/formoterol 80/4.5 (4-11 years)

My Regular Treatment Every Day:

(Write in or circle the number of doses prescribed for this patient)

Take [1, 2] inhalation(s) in the morning

and [0, 1, 2] inhalation(s) in the evening, every day

Reliever

Use 1 inhalation of budesonide/formoterol whenever needed for relief of my asthma symptoms

I should always carry my budesonide/formoterol inhaler

My asthma is stable if:

- I can take part in normal physical activity without asthma symptoms

AND

- I do not wake up at night or in the morning because of asthma

Other Instructions

_____

_____

Asthma Flare-up

If over a Period of 2-3 Days:

- My asthma symptoms are getting worse **OR NOT** improving

OR

- I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years or older) or more than 4 inhalations a day (if aged 4-11 years)

I should:

☒ Continue to use my regular everyday treatment **PLUS** 1 inhalation budesonide/formoterol whenever needed to relieve symptoms

☐ Start a course of prednisolone

☐ Contact my doctor

Course of Prednisolone Tablets:

Take _____mg prednisolone tablets

per day for _____days **OR**

_____

_____

If I need more than **12 budesonide/formoterol inhalations (total)** in any day (or more than 8 inhalations for children 4-11 years), I **MUST** see my doctor or go to the hospital the same day.

Asthma Emergency

Signs of an Asthma Emergency:

- Symptoms getting worse quickly
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- Little or no improvement from my budesonide/formoterol reliever inhalations

If I have any of the above danger signs, I should dial _____ for an ambulance and say I am having a severe asthma attack.

While I am waiting for the ambulance start my asthma first aid plan:

- Sit upright and stay calm.
- Take 1 inhalation of budesonide/formoterol. Wait 1-3 minutes. If there is no improvement, take another inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion).
- If only albuterol is available, take 4 puffs as often as needed until help arrives.
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance.
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack.

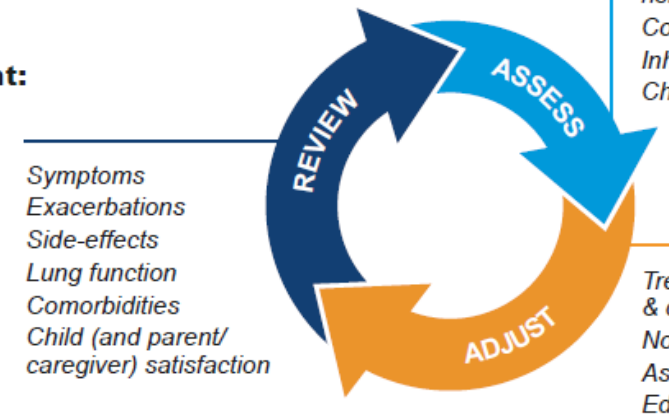
Modified from Australian action plan with permission from National Asthma Council Australia and AstraZeneca Australia

Supplement to Reddel et al, JACI in Practice 2022; 10: S31-s38

This template can be modified for other ICS-formoterol combinations or for as-needed-only ICS-formoterol.
The action plan on which it is based has been widely used in Australia and other countries since 2007.

GINA 2023 – Children 6–11 years

Personalized asthma management:
Assess, Adjust, Review



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Child and parent/caregiver preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Child (and parent/ caregiver) satisfaction

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

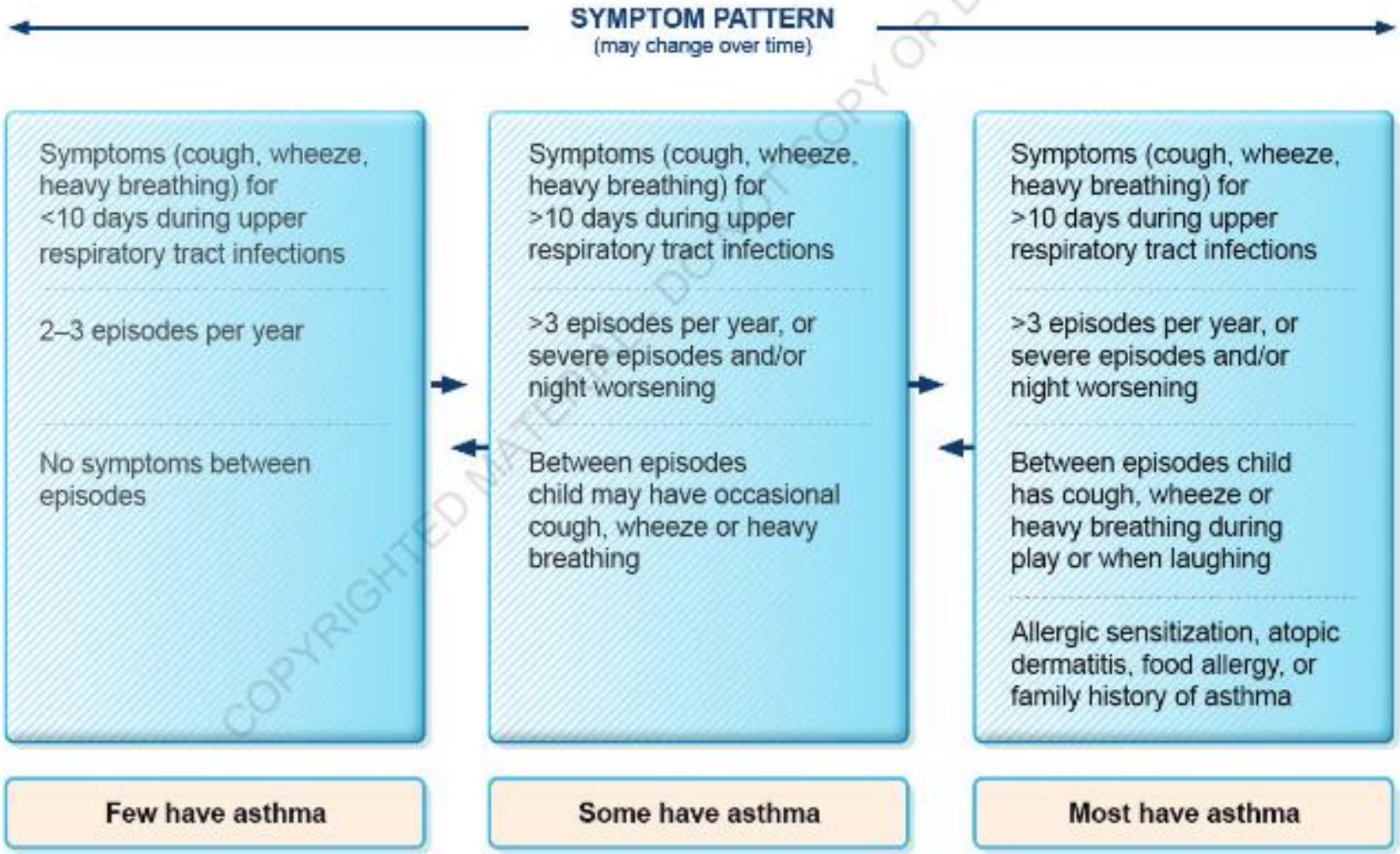
Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken*	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever (MART)	Medium dose ICS-LABA, OR low dose ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*As last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory relievers (AIR)

Box 3-13

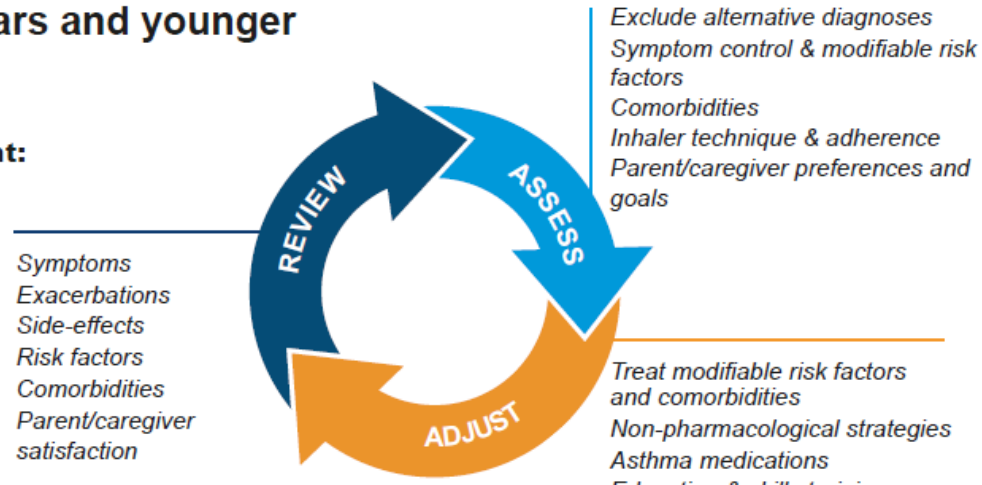
Box 6-1. Probability of asthma diagnosis in children 5 years and younger



Components of Severity		Classification of Asthma Severity (0–4 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0	1–2x/month	3–4x/month	>1x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2 exacerbations in 6 months requiring oral systemic corticosteroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time. → Exacerbations of any severity may occur in patients in any severity category.			
Recommended Step for Initiating Therapy (See figure 4–1a for treatment steps.)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, depending on severity, evaluate level of asthma control that is achieved. If no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternative diagnoses.			

GINA 2023 – Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE	*(Insufficient evidence for daily controller)*	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)	Double 'low dose' ICS *(See Box 6-7)*	Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral. Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Asthma diagnosis, and asthma not well-controlled on low dose ICS Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	Asthma not well-controlled on double ICS

Box 6-6

Difficult-to-treat and severe asthma

- Changes in GINA 2023
  - Double-blind study of withdrawal of mepolizumab in adults with severe eosinophilic asthma found more exacerbations in those who ceased mepolizumab than those who continued treatment *(Moore et al, ERJ 2022)*
  - Mepolizumab (anti-IL5) added as a Step 5 option for children 6–11 years with severe eosinophilic asthma *(Jackson et al, Lancet 2022)*
- Regardless of regulatory approvals, GINA recommends biologic therapy for asthma **only** if asthma is severe, and **only** if treatment has been optimized
- Head-to-head studies are needed
- Non-asthma indications for biologic therapy are mentioned only if the condition is relevant to asthma management, or if it is commonly associated with asthma
- Severe asthma guide published mid-2023 in large format

What is the new FDA approved drug for asthma?

Xolair was originally approved in 2003 to treat moderate to severe persistent allergic asthma in certain patients. The US Food and Drug Administration on Friday approved a medication called Xolair to help lessen the severity of an accidental allergic reaction in people who are allergic to multiple foods.

Why avoid antihistamines in asthma?

Reports in the literature have suggested that antihistamines are contraindicated in asthma because **they dry the secretions in the upper and lower respiratory tracts**.


You using your inhaler?
All the time. Go through one a week.
You sure you're using it right?
Do I look like an idiot?
No.
Why don't you show me how your inhaler works?
Hidden / 9GAG
Get 9GAG app on your iPhone!