

Catching Our Breath: Asthma Management Updates in Primary Care

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Disclosures

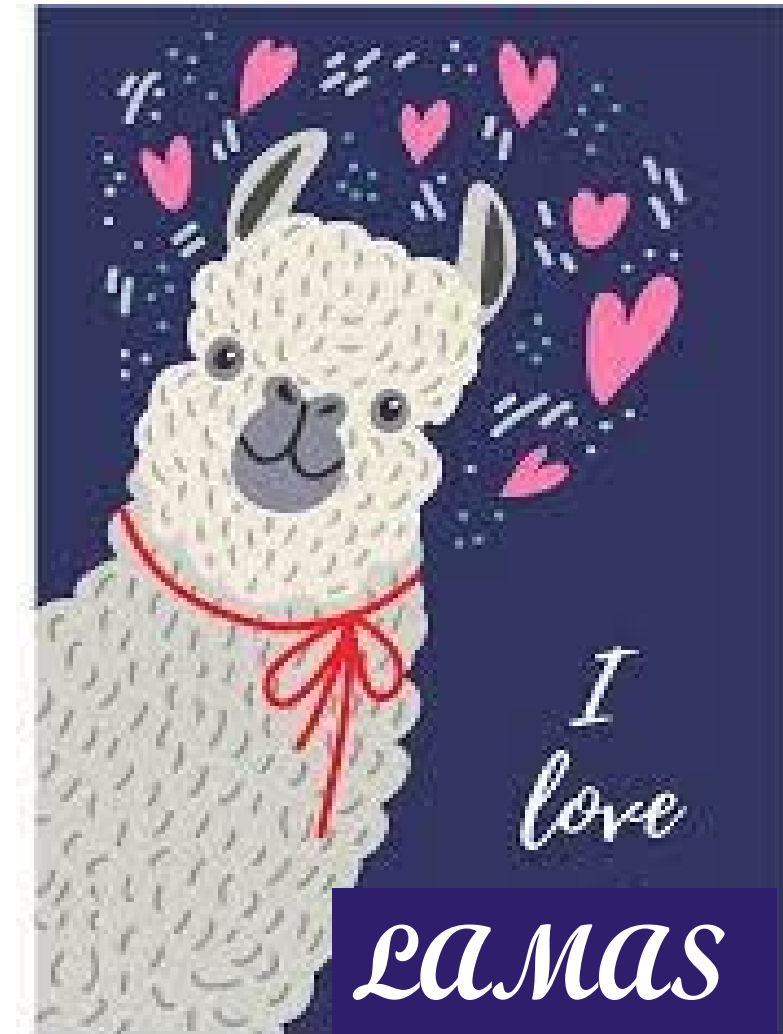
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Introduction

- New guidelines are complex
- Recommendations vary by age and step of therapy
- Highlight global concepts
- Cases

Common Abbreviations

- GINA-- Global Initiative for Asthma
- NAEPP– National Asthma Education & Prevention Program
- ICS– Inhaled corticosteroid
- LABA– Long-acting beta agonist (ex. salmeterol)
- SABA– Short acting beta agonist (ex. albuterol)
- LAMA– Long-acting muscarinic antagonist
- AIR– Anti-inflammatory reliever
- DPI– Dry powder inhaler
- MDI– Metered dose inhaler
- HFA- Hydrofluoroalkane (inhaler propellant)
- MART/ SMART– (Single) Maintenance And Reliever Therapy
- LTRA– Leukotriene receptor antagonist (ex. Montelukast or Singulair)



Background

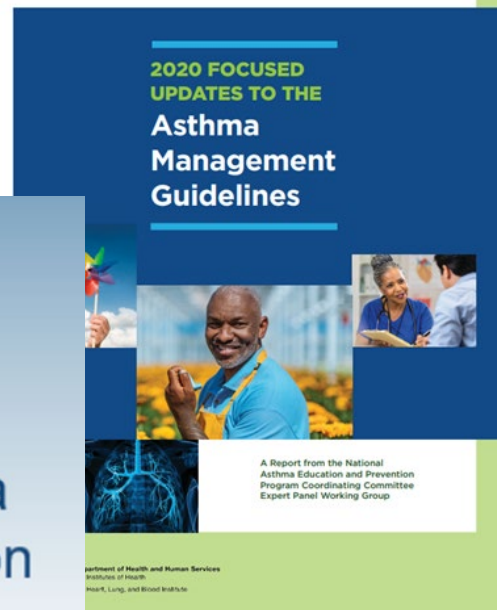
Two Sets of New Recommendations

GINA

- **Global Initiative for Asthma**
 - International committee
 - Primarily based in Europe
 - Annual updates
 - Most recent 2023



Global Strategy for Asthma
Management and Prevention



NAEPP (NHLBI)

- **National Asthma Education and Prevention Program**
 - US based
 - Responsible for the familiar guidelines that we know
 - Updated less frequently
 - 2007→2010→2020
 - Addressed 6 priority topics



Differences Between GINA and NAEPP

- **Age ranges slightly different**
 - NAEPP: 0-4, 5-11, 12+
 - GINA: 0-5, 6-11, 12+
- **Number of steps of therapy**
 - NAEPP 6 steps
 - GINA 5 steps
- **Use of high dose ICS in youngest age group**
- **NAEPP introduces ICS/LABA at younger age**

GINA Ages 6-11

Asthma medication options:

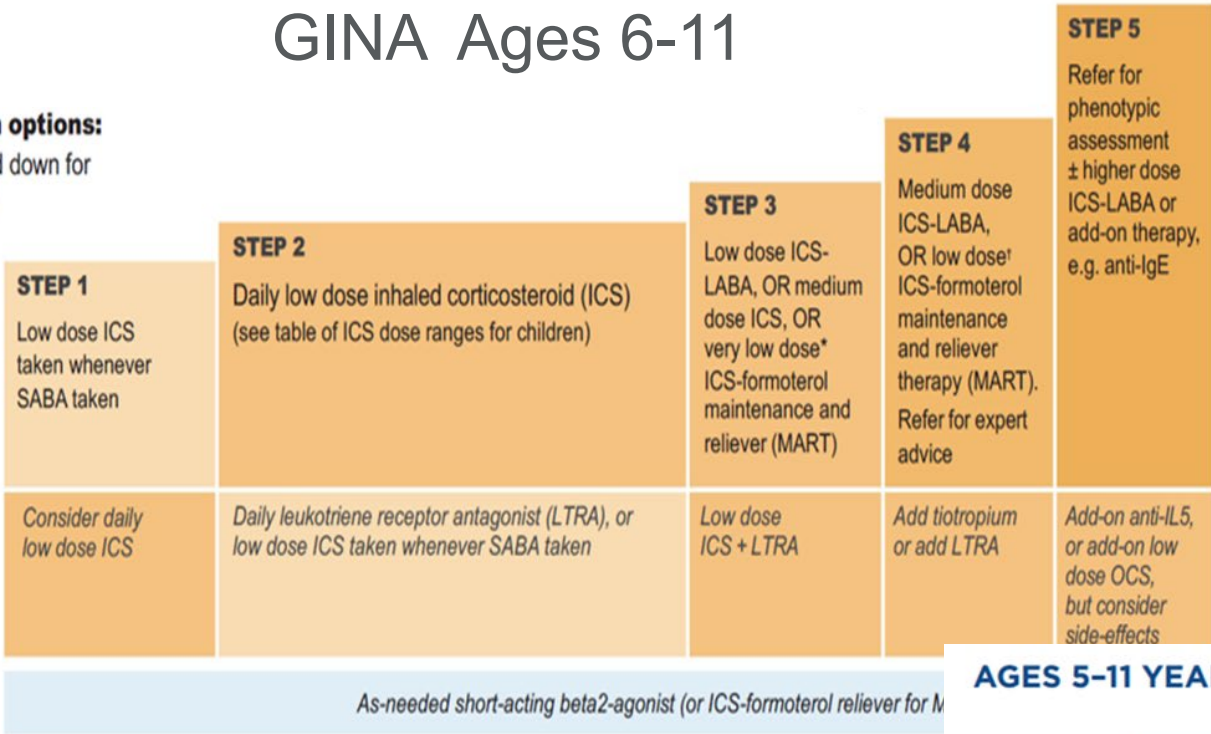
Adjust treatment up and down for individual child's needs

PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

Other controller options

RELIEVER



NAEPP

AGES 5-11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Both updates outline preferred and alternative tracks of management

Intermittent Asthma		Management of Persistent Asthma in Individuals Ages 5-11 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol ▲	Daily and PRN combination medium-dose ICS-formoterol ▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS + Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy ▲			Consider Omalizumab** ▲	

GINA



- Focus on controlling symptoms and ***reducing risk***
 - Death
 - Severe exacerbation
 - Side effects of medications



GINA Updates are Focused on Reduction of Risk

- Risks of albuterol alone as asthma treatment
 - Increased risk of *progression to severe exacerbation*
 - Increased risk of *severe exacerbation*
 - Increased risk of *death from asthma*
- Risks of use of high dose ICS in very young children even for short periods of time

Risks of SABA

- SABA alone even for short periods of time
 - β -receptor downregulation
 -  bronchodilator response
 -  bronchoprotection
 - Rebound bronchial hyperresponsiveness (Hancox, Respir Med 2000)
- Increased SABA use → higher risk of severe exacerbation and death from asthma (even with daily ICS)
 - > 3 canisters/yr incr exacerbation risk (Stanford, AAI, 2012; Nwaru, Eur Resp J, 2020)
 - > 12 canisters /yr incr risk of death (Suissa, AJRCCM, 1994, NEJM, 2000, 2002; Pauwels, Lancet 2003, Nwaru, Eur Resp J, 2020)

Old Concept

- Controller medication = inhaled steroids (+/- LABA)
- Reliever medication = albuterol (SABA)

New Concept: ICS and Rescue

- **ICS must be used EVEN in intermittent asthma**
- **Reliever medications for infrequent asthma***
 - Age 4-11 years: **Albuterol + inhaled steroids at the time of symptoms**
 - Age 12+ years: **ICS + formoterol at the time of symptoms**
 - Albuterol alone as rescue ONLY if taking daily ICS or ICS/LABA as maintenance

*GINA (NAEPP endorses albuterol alone in Step 1)

New Concept: ICS-formoterol as rescue

- As needed ICS-formoterol compared to
- Either prn SABA or daily ICS + prn albuterol
 - *Reduces severe exacerbations*
 - *Same or better reduction in EIB*
 - *Decreased ICS dose*
 - *Similar symptom control*

* For those previously only on SABA

Anti-inflammatory Reliever (AIR)

- **Steroids are part of the rescue regimen in mild asthma across all age groups**
 - Preschool—*high dose ICS with albuterol during URI*
 - School age—*ICS + albuterol prn symptoms*
 - Adolescents/adults—*ICS + formoterol prn*

Recommendations by Age:

Age 0-4 or 5 years

Case 1 3-year-old

- 4 episodes of wheezing in past year
- +eczema
- No admissions, 1 ED visit, Oral steroids x 2
- No symptoms when well
- Identified trigger is only URI
- Current regimen is albuterol prn

Case 1 3-year-old

- Is this child well controlled on current regimen?
- If not, what changes would you make?
 - Daily low dose inhaled steroids
 - Low dose ICS inhaler every time the child needs albuterol
 - Montelukast 4mg daily
 - High dose inhaled steroids and albuterol started at first sign of URI

Children 0-4 years of age--NAEPP

New recommendations:

- **Step 1** Intermittent ICS therapy (high dose ICS)
 - For children with recurrent wheezing, start 7–10-day course of daily high dose ICS + SABA at first sign of illness
- Step 2 Daily low dose ICS
- Step 3 Med dose ICS
- **Steps 4+** Daily ICS-LABA
- **For age 4 only:** (S)MART at step 3 and 4

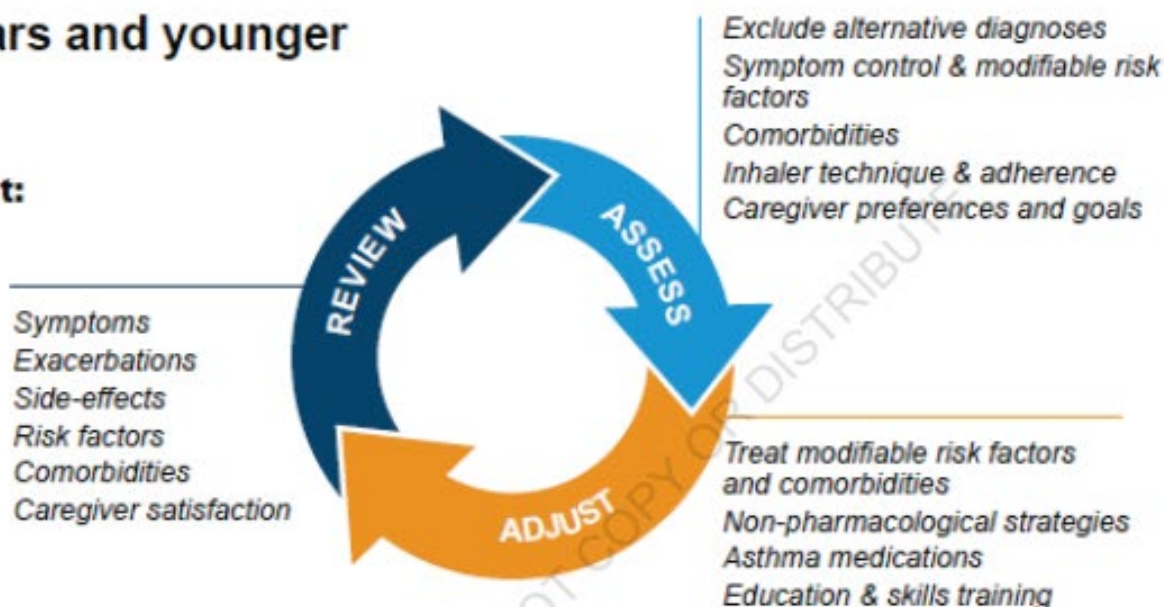
AGES 0-4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0-4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA▲ or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* + oral systemic corticosteroid and PRN SABA
For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5-11 Years diagram.						

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

PREFERRED CONTROLLER CHOICE

Other controller options (limited indications, or less evidence for efficacy or safety)

RELIEVER

CONSIDER THIS STEP FOR CHILDREN WITH:

STEP 1

(Insufficient evidence for daily controller)

Consider intermittent short course ICS at onset of viral illness

STEP 2

Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)

Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness

STEP 3

Double 'low dose' ICS (See Box 6-7)

Low dose ICS + LTRA
Consider specialist referral

STEP 4

Continue controller & refer for specialist assessment

Add LTRA, or increase ICS frequency, or add intermittent ICS

As-needed short-acting beta₂-agonist

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

Asthma not well-controlled on double ICS

Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures

Ages 0-4 or 5 Years: Step 1 or 2 Asthma Action Plan scenarios

- Step 1 Infrequent symptoms

Green Zone No daily medications

Rescue or Yellow Zone

Take Flovent 110mcg 2 puffs twice daily AND Albuterol 4 puffs q 4h prn

- Step 2 More frequent symptoms

Green Zone Taking Flovent 44mcg 1 puff twice daily

Rescue or Yellow Zone

Take Albuterol 4 puffs every 4 hours prn

Recommendations by Age:

Age 6-11 years

Case 2 10-year-old boy

- Mild persistent asthma
- Current therapy:
 - fluticasone 44mcg 2 puffs twice daily
 - Increases to 4 puffs twice daily and adds albuterol prn during URI
- Today presents with increased frequency of asthma symptoms over the past 6 weeks
 - Good adherence to daily fluticasone
 - Good MDI and spacer technique

Case 2 10-year-old boy

- What changes would you make?
 - Increase daily maintenance med from low dose to medium dose ICS
 - Change daily controller from fluticasone to ICS/LABA such as budesonide-formoterol or fluticasone-salmeterol and continue SABA as reliever
 - Initiate (S)MART with budesonide-formoterol 80/4.5 (2 puffs once daily and 1 puff as needed)
- If this child was well controlled, are changes needed?

Children 6-11 years of age

New recommendations:

- **Step 1 Low dose ICS + albuterol prn symptoms**
- **Step 2 Daily low dose ICS + prn albuterol**

- **Steps 3, 4**

ICS-formoterol daily *AND* as needed = SMART

OR

Daily ICS-formoterol + prn albuterol

OR

Medium dose ICS + prn albuterol

- **Step 5 NO SMART**

(S)MART: (Single) Maintenance And Reliever Therapy

- Budesonide/formoterol (Symbicort, Breyna, generic)
- Mometasone/formoterol (Dulera)



Not All LABAs are the Same!

FORMOTEROL: rapid onset of action AND extended length of action

ICS/formoterol

- can serve as rescue and controller
- now known as an anti-inflammatory reliever
- most data with budesonide/formoterol

ANTI-INFLAMMATORY RELIEVER = AIR

(ICS+SABA inhaler approved for ≥ 18 yrs which is also AIR)

Children 6-11 years of age

New recommendations:

- **Step 1 Low dose ICS + albuterol prn symptoms**
- **Step 2 Daily low dose ICS + prn albuterol**

- **Steps 3, 4**

ICS-formoterol daily *AND* as needed = SMART

OR

Daily ICS-formoterol + prn albuterol

OR

Medium dose ICS + prn albuterol

- **Step 5 NO SMART**

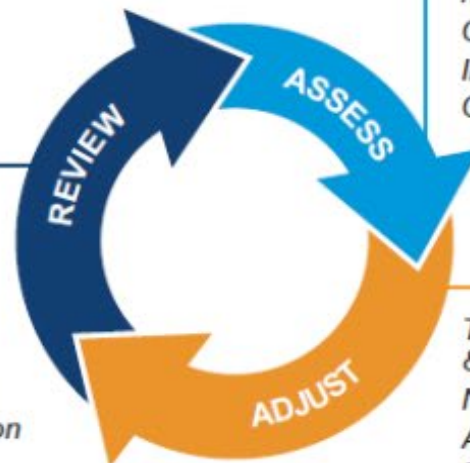
GINA 2023 – Children 6–11 years



Personalized asthma management:

Assess, Adjust, Review

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



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

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

PREFERRED CONTROLLER

to prevent exacerbations
and control symptoms

Other controller options
(limited indications, or
less evidence for efficacy
or safety)

STEP 1

Low dose ICS
taken whenever
SABA taken*

Consider daily
low dose ICS

STEP 2

Daily low dose inhaled corticosteroid (ICS)
(see table of ICS dose ranges for children)

Daily leukotriene receptor antagonist (LTRA), or
low dose ICS taken whenever SABA taken*

STEP 3

Low dose ICS-
LABA, OR medium
dose ICS, OR
very low dose
ICS-formoterol
maintenance and
reliever (MART)

Low dose
ICS + LTRA

STEP 4

Medium dose
ICS-LABA,
OR low dose
ICS-formoterol
maintenance and
reliever therapy
(MART).
Refer for expert
advice

Add tiotropium
or add LTRA

STEP 5

Refer for
phenotypic
assessment
± higher dose
ICS-LABA or
add-on therapy,
e.g. anti-IgE,
anti-IL4Rα,
anti-IL5

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)

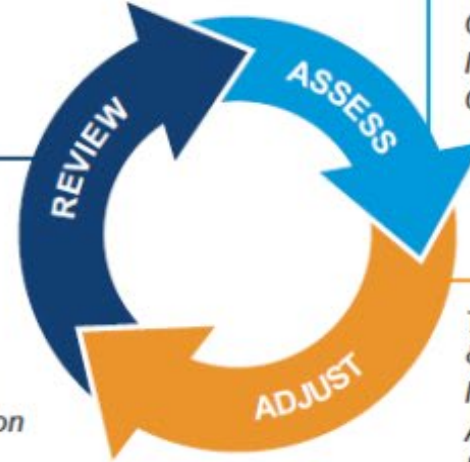
GINA 2023 – Children 6–11 years



Personalized asthma management:

Assess, Adjust, Review

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



Confirmation of diagnosis if necessary
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Comorbidities
Inhaler technique & adherence
Child and parent/caregiver preferences and goals

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

Asthma medication options:

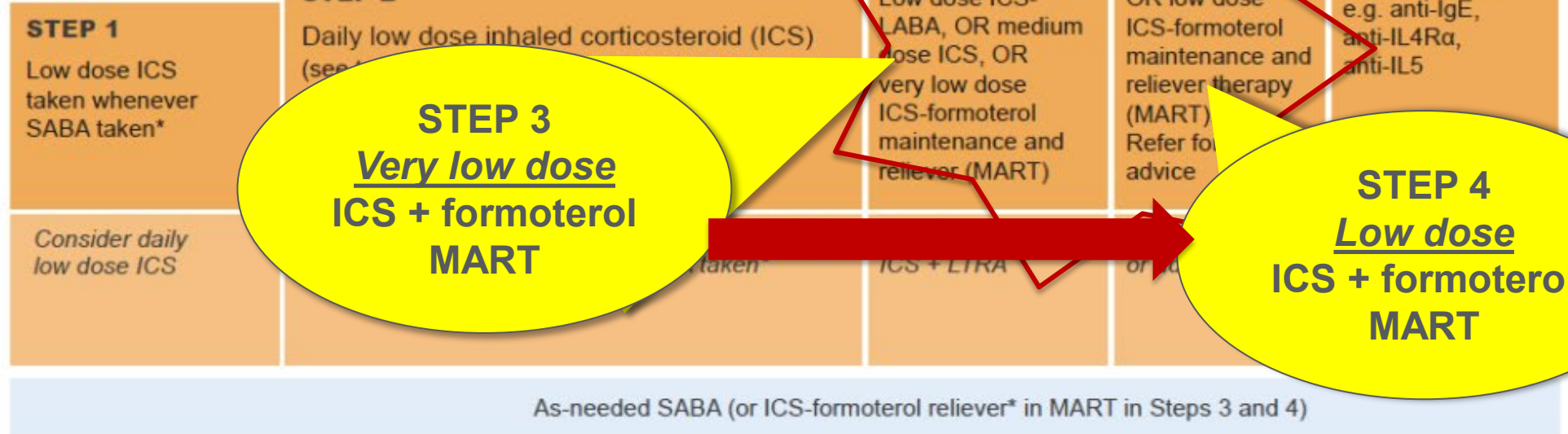
Adjust treatment up and down for
individual child's needs

PREFERRED CONTROLLER

to prevent exacerbations
and control symptoms

Other controller options
(limited indications, or
less evidence for efficacy
or safety)

RELIEVER



*Anti-inflammatory relievers (AIR)

Important (S)MART Points!!

- ICS/LABA must include *formoterol*
- Maintenance dose in SMART is 1-2 puffs
- Very low dose is 1 puff budesonide/formoterol 80/4.5
- Low dose is 1 puff budesonide/formoterol 160/4.5
- Rescue dose in SMART is 1 puff
- ***NO SMART FOR STEP 5 or Severe Asthma***

More updates for ages 5 or 6-11 years

- *No specific amount of time between rescue doses for SMART*
- *Maximum number of puffs per day = 8 (age 5-11)*
- *Dose of ICS-formoterol is lower if using SMART*

STEP 4	SMART	NOT SMART	
Maintenance	<u>Very low dose</u> ICS-formoterol	<u>Low dose</u> ICS- formoterol	Medium dose ICS
Reliever	<u>Very low dose</u> ICS-formoterol <i>Max 8 puffs per day</i>	Albuterol prn	Albuterol prn

More updates for ages 5 or 6-11 years

- **Albuterol is the reliever UNLESS using SMART**
- Consider tiotropium at Step 4
- Step 4,5 refer for expert advice +/- biologic

Ages 5-6 to 11 Years: Step 4 Asthma Action Plan scenarios

Green Zone Take Symbicort 80/4.5 2 puffs twice daily

Rescue or Yellow Zone

Take Albuterol 4 puffs with spacer every 4 hours

OR **SMART**



Green Zone Take Symbicort 80/4.5 1 puff twice daily

Rescue or Yellow Zone

Take Symbicort 80/4.5 1 puff as needed up to maximum of 8 puffs per day (including Green Zone puffs)

Ages 5 or 6 to 11 Years: Step 5 Asthma Action Plan scenarios

Green Zone Take Advair 230/21 1 puff twice daily

Rescue or Yellow Zone

Take Albuterol 4 puffs q 4 hours prn

OR

Green Zone Take Breo 100/25 1 puff once daily

Rescue or Yellow Zone

Take Albuterol 4 puffs q 4 hours prn

Recommendations by Age: Age 12 years and older

Case 3 14-year-old female

- History of mild persistent asthma, well controlled on mometasone (Asmanex) 110mcg 1 puff twice daily (low dose ICS) and albuterol prn.
- Has mild exacerbations during Spring and Fall
- Has been worse this Winter and required one course of oral steroids

Case 3 14-year-old female

- Is a change in therapy needed?

≥ 12 years of age

New recommendations:

- **Steps 1-2: As needed low dose ICS + formoterol**
- **Steps 3, 4:**
ICS-formoterol daily *AND* as needed = SMART
OR
Daily ICS-formoterol + albuterol
- **Step 5: ICS-formoterol daily + LAMA + prn albuterol**
Add biologic

≥ 12 years of age

New recommendations:

- ICS-formoterol is preferred *reliever*
- ICS-formoterol is preferred *maintenance*
- This approach **reduces severe exacerbations across all treatment steps compared with using albuterol as reliever**

SMART in age 12+ years

- **Maintenance** dose in SMART is 1-2 puffs
- Starting dose is low dose budesonide-formoterol
- **Rescue** dose is always 1 puff of low dose budesonide-formoterol
- Maximum number of puffs per day is 12 puffs (including maintenance puffs)
- ***No specific amount of time between rescue doses for SMART***

More updates for ages 12+ years

- *Dose of ICS-formoterol is lower if using SMART*

STEP 4	SMART	NOT SMART	
Maintenance	<u>Very low dose</u> ICS-formoterol	<u>Low dose</u> ICS- formoterol	Medium dose ICS
Reliever	<u>Very low dose</u> ICS-formoterol <i>Max 8 puffs per day</i>	Albuterol prn	Albuterol prn

- If not using ICS-formoterol for maintenance →
albuterol should be reliever

Benefits of ICS/formoterol as reliever

- ICS-formoterol used as a reliever with or without maintenance ICS-formoterol is the preferred treatment approach for children 12+ years of age and adults.
- This approach **reduces severe exacerbations across all treatment steps compared with using albuterol as reliever.**

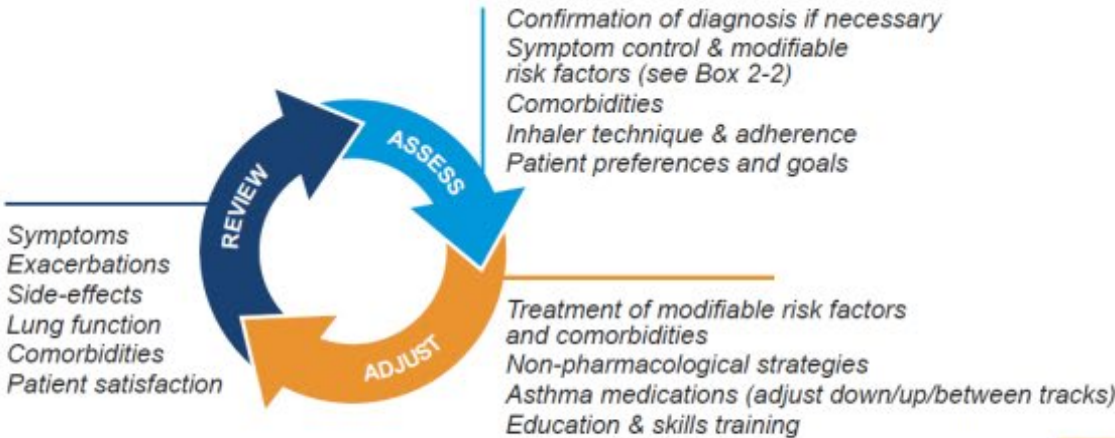
Age Based Doses for AIR & SMART

Step	Age (years)	Medication and strength (per 2 puffs of pMDI)	Dosage (number of puffs)
Steps 1-2 (AIR only)	6 - 11 12 - 17 >18	NO EVIDENCE TO DATE Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	1 puff whenever needed
Step 3 ((S)MART)	6 – 11 12 - 17 >18	Budesonide-formoterol 80/4.5 Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	1 puff once or twice daily (once daily for children), PLUS 1 puff whenever needed
Step 4 ((S)MART)	6 – 11 12 - 17 >18	Budesonide-formoterol 80/4.5 Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	2 puffs twice daily (1 puff twice daily for children), PLUS 1 puff whenever needed
Step 5-6 ((S)MART)	6 – 11 12 - 17 >18	NOT RECOMMENDED Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	2 puffs twice daily, PLUS 1 puff whenever needed

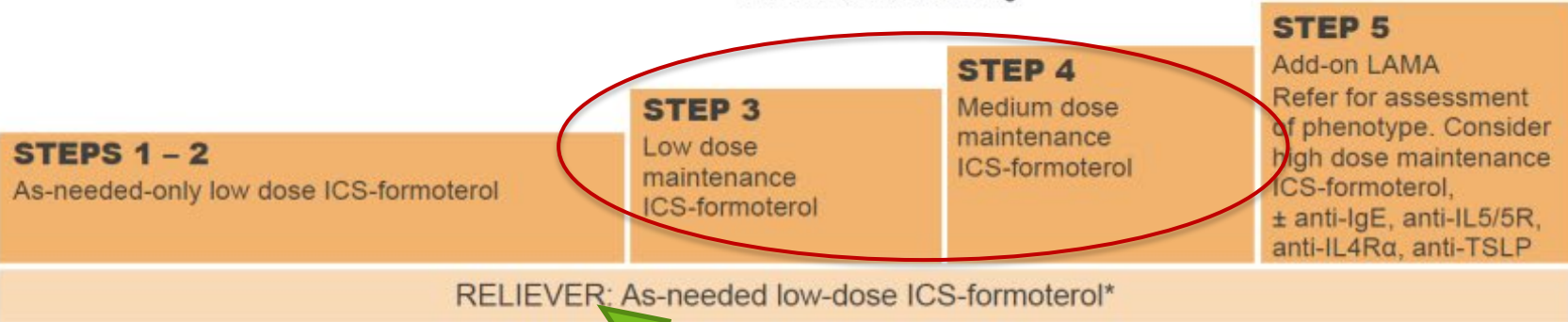
*Table adapted from GINA 2023, Box 3-15, p. 80. Available at ginasthma.org.

GINA 2023 – Adults & adolescents 12+ years

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

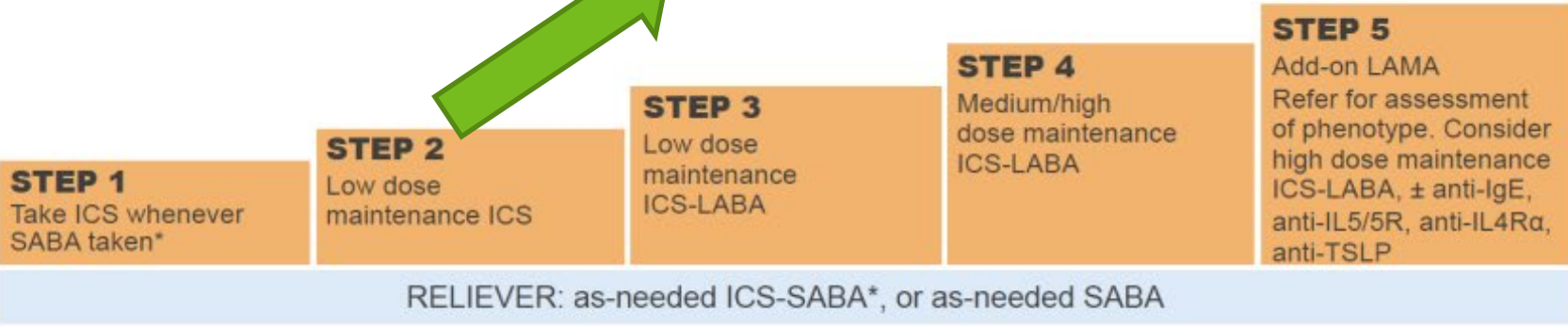


TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen



See GINA severe asthma guide

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



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
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*Anti-inflammatory reliever (AIR)

≥ 12 years of age

(S)MART therapy preferred, but not the only option

- Daily low dose ICS-LABA with albuterol as reliever
- If any ICS-LABA other than ICS-formoterol is maintenance → albuterol should be reliever
- Decision about implementing SMART should take multiple factors into account

Limitations to implementation of SMART

- *Intermittent ICS use may be less efficacious in patients with low or high perception of asthma symptoms*
 - Too rare or too frequent use of ICS
- Cost of medications/insurance coverage
- Need for increased volume of medication per month with SMART
- Patient/family preference
- Patient/family understanding
- Medication intolerance

What's Good About MART?

- It uses a single inhaler for both maintenance and reliever which is less confusing for patients
- A patient's treatment can be stepped up or down according to clinical need without changing the medication or device.
- This cannot be done with any other ICS-LABA combination except ICS-formoterol.
- ICS-formoterol can also be used prior to exercise or allergen exposure.

Age 12+: Step 4

Asthma Action Plan scenarios

Green Zone Take Symbicort 160/4.5 2 puffs with spacer twice daily

Rescue or Yellow Zone

Take Albuterol 4 puffs with spacer every 4 hours

OR **SMART** 

Green Zone Take Symbicort 160/4.5 2 puffs with spacer twice daily

Rescue or Yellow Zone

Take Symbicort 160/4.5 1 puff as needed up to maximum of 12 puffs per day (including Green Zone puffs)

Age 12+: Step 4

Asthma Action Plan scenarios

Green Zone Take Breo 200 1 puff once daily

Rescue or Yellow Zone

Take Albuterol 4 puffs with spacer every 4 hours

OR **SMART** 

Green Zone Take Dulera 100/5 2 puffs with spacer twice daily

Rescue or Yellow Zone

Take Dulera 100/5 1 puff as needed up to maximum of 12 puffs per day (including Green Zone puffs)

New Management Strategy Reduces Risk

- ***Steps 1-2 (AIR only): low dose ICS-formoterol is used as needed for symptom relief without any maintenance treatment.***
 - **Reduces risk of severe exacerbations and ED visits/admissions by 65% compared with SABA alone**
 - **Reduces risk of severe exacerbations and ED visits/admissions by 37% compared to daily ICS with SABA as reliever.** Starting ICS-formoterol as reliever avoids training patients to regard SABA as their main asthma treatment.
- ***Steps 3-5 (S)MART): maintenance and reliever therapy with ICS-formoterol***
 - **Reduces risk of severe exacerbations by 32% compared with the same dose of ICS-LABA**
 - **Reduces risk by 23% compared with higher dose ICS-LABA**
 - **Reduces risk by 17% compared with the usual care.**
- (S)MART is also an option for children ages 6-11 in Steps 3-4

Summary of Major Changes

- No albuterol alone for asthma management even in mild asthma
- Mild asthma anti-inflammatory *reliever*:
 - 0-5yr: high dose ICS + albuterol x 7-10 days with URI
 - 6-11yr: Low dose ICS + albuterol prn in step 1
 - 12+ yr: Low dose ICS-formoterol in steps 1,2
- (S)MART with ICS-formoterol in steps 3 & 4 in age > 5
- Use of ICS-formoterol alone as rescue medication for age ≥ 12
- NAEPP—SMART steps 3,4 only across all ages

NAEPP Reliever Philosophy

- Albuterol alone as rescue in Step 1 for ages 5+
- Albuterol is preferred reliever except in SMART
- Don't endorse as needed prn ICS + SABA until age 12 as alternative to daily low dose ICS + prn SABA
- Don't endorse ICS-formoterol as reliever except as part of SMART
- (S)MART with ICS-formoterol in steps 3 & 4 in age ≥ 4

NAEPP and GINA Agree

If the patient is *well controlled* on current regimen that includes inhaled steroids as maintenance therapy and short acting beta-agonist as rescue,

THERE IS NO NEED TO ALTER THERAPY

Case 1 3-year-old

- 4 episodes of wheezing in past year
- +eczema
- No admissions, 1 ED visit, Oral steroids x 2
- No symptoms when well
- Identified trigger is only URI
- Current regimen is albuterol prn

Case 1 3-year-old

- Is this child well controlled on current regimen?
- If not, what changes would you make?
 - Daily low dose inhaled steroids
 - Low dose ICS inhaler every time the child needs albuterol
 - Montelukast 4mg daily
 - High dose inhaled steroids and albuterol started at first sign of URI

Case 1 Debrief

- Best answer: High dose inhaled steroids and albuterol started at first sign of URI and continue x 7-10 days
- Daily low dose inhaled steroids
- 2 puffs of ICS inhaler every time the child needs albuterol
- Montelukast 4mg daily
- NAEPP: conditional recommendation with high certainty
- GINA: *consider* short course of high dose ICS with URI

Case 1 Debrief

- Daily low dose inhaled steroids---A possible best answer
 - if family unable to recognize early symptoms
 - If family better with everyday routine
- 2 puffs of ICS inhaler every time the child needs albuterol
 - Not recommended in this age group
 - No data in < 4 yr old
 - Regimen recommended for step 1 in 6-11 year olds (GINA), step 2 for 12+ (NAEPP)
- Montelukast 4mg daily
 - Not as effective as ICS
 - Risk of neuropsychiatric side effects

Case 2 10-year-old boy

- Mild persistent asthma
- Current therapy:
 - fluticasone 44mcg 2 puffs twice daily
 - Increases fluticasone to 4 puffs twice daily and adds albuterol prn during URI
- Today presents with increased frequency of asthma symptoms over the past 6 weeks
 - Good adherence to daily fluticasone
 - Good MDI and spacer technique

Case 2 10-year-old boy

- What changes would you make?
 - Increase daily maintenance med from low dose to medium dose ICS
 - Change daily controller from fluticasone to ICS/LABA such as budesonide-formoterol or fluticasone-salmeterol and continue SABA as reliever
 - Initiate (S)MART with budesonide-formoterol 80/4.5 (2 puffs once daily and 1 puff as needed)

Case 2 Debrief

- Best option based on NAEPP & GINA: **Initiate (S)MART with budesonide-formoterol 80/4.5 (2 puffs once daily and 1 puff as needed)**
 - Step up from step 2 (low dose ICS)→Step 3 (ICS-LABA)
 - Step 3 preferred use of ICS LABA is SMART
- Evidence that ICS-formoterol as rescue decreases risk of progression to severe exacerbation, admission, death compared to SABA alone **across all asthma severities**
- If this child was well controlled, are changes needed?
NO, if child well controlled on daily ICS and prn SABA

Case 2 Debrief

- Best option based on NAEPP & GINA: **Initiate (S)MART with budesonide-formoterol 80/4.5 (2 puffs once daily and 1 puff as needed)**
- Step up from step 2 (low dose ICS)→Step 3 (ICS-LABA)
- Step 3 preferred use of ICS LABA is SMART
- ICS-formoterol as rescue decreases risk of progression to severe exacerbation, admission, death compared to SABA **across all asthma severities**

Case 2 Debrief

- Change daily controller from fluticasone to ICS/LABA such as budesonide-formoterol or fluticasone-salmeterol and continue SABA as reliever—*A possible best answer*
 - *if ICS-formoterol is not covered by insurance*
 - *If insurance will not cover enough inhalers per month for SMART*
 - *If family has difficulty understanding concept*
- Remember if using ICS-LABA that does not contain formoterol, albuterol is the rescue
- Increase daily maintenance med from low dose to medium dose ICS—*Acceptable alternative*

Caveats about (S)MART

- Evidence supports its use
- Must be ICS-formoterol
 - Budesonide-formoterol (Symbicort, Breyna)
 - Mometasone-formoterol (Dulera)
- Not necessarily the best regimen for all families or situations
 - Insurance does not cover ICS-formoterol
 - Insurance will not cover 2 ICS-formoterol inhalers (e.g. 1 for home, 1 for school)
 - Maintenance dose of 2 puffs twice daily = 1 inhaler, need a 2nd inhaler to have any rescue puffs
 - Family preference, uncomfortable with paradigm shift

Caveats about (S)MART

- Easiest scenario:
 - When maintenance is 1 puff twice daily
 - Child old enough to self carry at school or home schooled
- Workaround
 - Use ICS-formoterol (S)MART therapy at home
 - Have SABA available as rescue at school

Case 2 Debrief

- If this child was well controlled, are changes needed? **Yes**
- **NAEPP *DOES NOT* recommend increasing dose of ICS monotherapy with SABA during exacerbations**
(Low level of evidence supporting this practice)
- If well controlled, recommendation = continue daily low dose ICS and add SABA for rescue

Case 3 14-year-old female

- History of mild persistent asthma, well controlled on mometasone (Asmanex) 110mcg 1 puff twice daily (low dose ICS) and albuterol prn.
- Has mild exacerbations during Spring and Fall
- Has been worse this Winter and required one course of oral steroids

Case 3 14-year-old female

- Is a change in therapy needed?

Case 3 Debrief

- Patient is well controlled so no change in therapy is needed
- However new NAEPP guidelines offer an alternative therapy in children ≥ 12 years old with well controlled mild persistent asthma (Step 2)
 - As needed ICS + SABA taken together for symptoms
 - GINA guidelines: could step down to ICS/formoterol as needed
 - Not a good option for poor perceivers

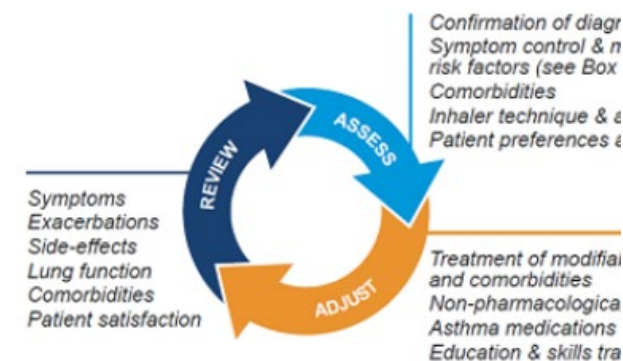
AGES 12+ YEARS: STEPWISE APPROACH FOR

	Intermittent Asthma	Management of Persistent Asthma		
Treatment	STEP 1	STEP 2	STEP 3	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA ▲	Daily and PRN combination low-dose ICS-formoterol ▲	
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, ▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



TRACK 1: PREFERRED CONTROLLER and RELIEVER

Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2

As-needed-only low dose ICS-formoterol

STEP 3

Low dose maintenance ICS-formoterol

RELIEVER: As-needed low-dose ICS-

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

Take ICS whenever SABA taken*

STEP 2

Low dose maintenance ICS

STEP 3

Low dose maintenance ICS-LABA

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

References

- Global Initiative for Asthma (GINA) www.ginasthma.org
 - Pocket Guide
 - Slides
- National Asthma Education and Prevention Program (NAEPP) www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates
 - At-A-Glance-Guide
 - Clinician's Guide
- NAEPP updates: Cloutier, et. al. *JACI*, 2020

NAEPP 2020 Focused Updates to Asthma Management

AGES 0-4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0-4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily medium-dose ICS and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* + oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5-11 Years diagram.			

NAEPP 2020 Focused Updates to Asthma Management

AGES 5-11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5-11 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS + Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

NAEPP 2020 Focused Updates to Asthma Management

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 [■]
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

GINA 2023 – Children 5 years and younger



Personalized asthma management:

Assess, Adjust, Review response

Symptoms
Exacerbations
Side-effects
Risk factors
Comorbidities
Parent/caregiver satisfaction



Exclude alternative diagnoses
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Parent/caregiver preferences and goals

Treat modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications
Education & skills training

Asthma medication options:

Adjust treatment up and down for individual child's needs

PREFERRED CONTROLLER CHOICE

Other controller options (limited indications, or less evidence for efficacy or safety)

RELIEVER

CONSIDER THIS STEP FOR CHILDREN WITH:

STEP 1 (Insufficient evidence for daily controller)	STEP 2	STEP 3	STEP 4
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	
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
As-needed short-acting beta ₂ -agonist			
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

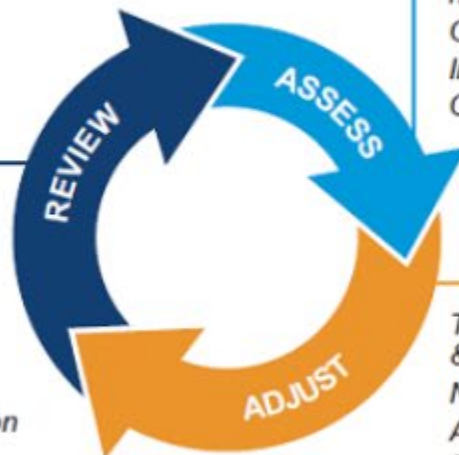
GINA 2023 – Children 6–11 years



Personalized asthma management:

Assess, Adjust, Review

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



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

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

PREFERRED CONTROLLER

to prevent exacerbations
and control symptoms

Other controller options
(limited indications, or
less evidence for efficacy
or safety)

STEP 1

Low dose ICS
taken whenever
SABA taken*

Consider daily
low dose ICS

STEP 2

Daily low dose inhaled corticosteroid (ICS)
(see table of ICS dose ranges for children)

Daily leukotriene receptor antagonist (LTRA), or
low dose ICS taken whenever SABA taken*

STEP 3

Low dose ICS-
LABA, OR medium
dose ICS, OR
very low dose
ICS-formoterol
maintenance and
reliever (MART)

Low dose
ICS + LTRA

STEP 4

Medium dose
ICS-LABA,
OR low dose
ICS-formoterol
maintenance and
reliever therapy
(MART).
Refer for expert
advice

Add tiotropium
or add LTRA

STEP 5

Refer for
phenotypic
assessment
± higher dose
ICS-LABA or
add-on therapy,
e.g. anti-IgE,
anti-IL4Rα,
anti-IL5

As last resort,
consider add-on
low dose ICS, but
consider side-effects

RELIEVER

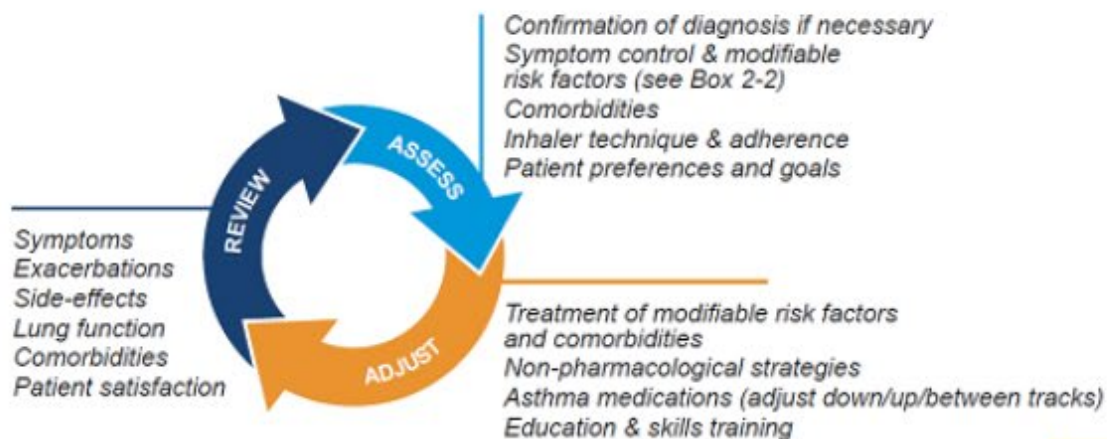
As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)

*Anti-inflammatory relievers (AIR)

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



TRACK 1: PREFERRED CONTROLLER and RELIEVER

Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2

As-needed-only low dose ICS-formoterol

STEP 3

Low dose maintenance ICS-formoterol

STEP 4

Medium dose maintenance ICS-formoterol

STEP 5

Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

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

Take ICS whenever SABA taken*

STEP 2

Low dose maintenance ICS

STEP 3

Low dose maintenance ICS-LABA

STEP 4

Medium/high dose maintenance ICS-LABA

STEP 5

Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

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

*Anti-inflammatory reliever (AIR)

Review of the Evidence

Track 1, Steps 1–2: As-needed-only low-dose ICS-formoterol

COMPARED WITH AS-NEEDED SABA

- § Two studies (*SYGMA 1*, O'Byrne et al, *NEJM* 2018, n=3836; *Novel START*, Beasley et al, *NEJM* 2019, n=668)
- § Risk of severe exacerbations was reduced by 60–64% (*SYGMA 1*, *Novel START*)

COMPARED WITH MAINTENANCE LOW DOSE ICS plus as-needed SABA

- § Four studies (*SYGMA 1*; *SYGMA 2*, Bateman et al, *NEJM* 2018, n=4176; *Novel START*; *PRACTICAL*, Hardy et al, *Lancet* 2019, n=885)
- § Risk of severe exacerbations similar (*SYGMA 1 & 2*), or lower (*Novel START*, *PRACTICAL*)
- § Symptoms very slightly more, e.g. ACQ-5 0.15 (vs 0.5 MCID), not worsening over 12 months
- § Pre-BD FEV₁ slightly lower (~54 mL), not worsening over 12 months
- § FeNO slightly higher (10ppb), not increasing over 12 months (*Novel START*, *PRACTICAL*)
- § As-needed ICS-formoterol used on ~ 30% of days à average ICS dose ~50–100mcg budesonide/day
- § Benefit independent of T2 status, lung function, exacerbation history (*Novel START*, *PRACTICAL*)
- § Qualitative research: most patients preferred as-needed ICS-formoterol (*Baggott Thorax* 2020, *ERJ* 2020; *Foster Respir Med* 2020, *BMJ Open* 2022)

*Budesonide-formoterol 200/6 [160/4.5] mcg by Turbuhaler, 1 inhalation as needed for symptom relief

Track 1, Steps 1–2: As-needed-only low-dose ICS-formoterol



- n Risk of severe exacerbations (*Crossingham et al, Cochrane 2021*)
 - § Compared with as-needed SABA alone: **55% reduction** (OR 0.45 [0.34–0.60])
 - § Compared with daily ICS plus as-needed SABA: (OR 0.79 [0.59–1.07])
- n Risk of emergency department visits or hospitalizations (*Crossingham et al, Cochrane 2021*)
 - § Compared with as-needed SABA alone: **65% reduction** (OR 0.35 [0.20–0.60])
 - § Compared with daily ICS plus as-needed SABA: **37% reduction** (OR 0.63 [0.44–0.91])
 - § Large population-level reduction in healthcare utilization

Track 2, Steps 1–2: As-needed-only ICS-SABA



Combination as-needed ICS-SABA

- n BEST study, combination BDP-albuterol (*Papi et al, NEJMed 2007, n=445, 6 months*)
 - § Mean number of exacerbations per patient per year lower with as-needed combination (0.74) and regular BDP (0.71) compared with as-needed albuterol (1.63, $P<0.001$) and regular combination BDP-albuterol (1.76, $P<0.001$)

Taking ICS whenever SABA taken with separate inhalers

- n TREXA study, BDP and albuterol, children and adolescents (*Martinez et al, Lancet 2011, n=288, 9 months*)
 - § Frequency of exacerbations highest with albuterol alone (49%); lower with daily BDP (28%, $p=0.03$), daily plus as-needed BDP and SABA (31%, $p=0.07$) and as-needed BDP+SABA (35%, $p=0.07$)
 - § Growth 1.1cm less in daily and combined groups but not as-needed-only group
- n BASALT study, BDP and albuterol, adults (*Calhoun et al, JAMA 2012, n=342, 9 months*)
 - § Similar exacerbations with as-needed BDP+SABA as with 6-weekly physician-adjusted or FeNO-adjusted ICS
- n ASIST study, BDP and albuterol, African-American children and adolescents (*Sumino et al, Annals ATS 2020, n=206, 12 months*)
 - § Similar symptoms control and exacerbations compared with physician-adjusted ICS

ICS + SABA as rescue: mild persistent asthma

TREXA study

- 5-18 years
- Mild persistent asthma
- Control with low dose ICS

Daily beclomethasone
+
Prn ICS + SABA

- Decr time to exac

Daily beclomethasone
+
Prn SABA

- Decr time to exac

Prn SABA

- Improved growth cf daily ICS
- Decr treatment failure

ICS + SABA as rescue: mild asthma

Symptom based vs MD based dosing of ICS

Low dose ICS

+

Prn ICS + SABA

- ACT
- Exacerbations
- Lung function
- **Lower total ICS dose**



Low dose ICS

+

Prn SABA

- ACT
- Exacerbations
- Lung function

- AA children
- 6-17 years
- Control with low dose ICS

SMART in children 4-11 years old

STAY study

Low dose bud + form
Prn bud + form

- **Decr risk of severe exac by**
 - 79% from high dose
 - 70% from low dose
- **Fewer symptoms**
- **Better growth**

Low dose bud + form
Prn SABA

- **More symptoms**
- **More severe exacerbations**

High dose bud + form
Prn SABA

- **Decreased growth**
- **More symptoms**
- **More severe exacerbations**