CHICAGO ASTHMA CONSORTIUM KICK ASTHMA FORUM- NEW ASTHMA GUIDELINES

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HOW DID THESE GUIDELINES COME ABOUT

An Expert Panel coordinated by the NHLBI of the NIH convened July 2018 to examine six priority topics after a needs assessment was conducted.

Using the Grading of Recommendations, Assessment, Development, and Evaluation framework, the Expert Panel made 19 recommendations for three age groups (0–4 yr, 5–11 yr, and 12 yr or older) based on studies published through October 2018

6 TOPICS INCLUDED

- Intermittent inhaled corticosteroids (ICS)
- Add-on inhaled long-acting muscarinic antagonists
- Bronchial thermoplasty
- Indoor allergen mitigation strategies
- Immunotherapy
- Use of fractional exhaled nitric oxide

WHY IS THE GLOBAL INITIATIVE FOR ASTHMA REPORT (GINA) ANY DIFFERENT?

The GINA report is intended to inform a comprehensive global strategy for various aspects of diagnosis and management of mild to severe asthma, including in low- and middle-income countries.

The NAEPP updates were for the 6 topics previously discussed.

TABLE II. Differences between the GINA and NAEPP approaches to asthma management*

Approach	GINA	NAEPP
Direction	Global	National
Composition	Primarily asthma specialists from representative countries	Multidisciplinary combination of asthma specialists, primary care physicians, health policy experts, implementation and dissemination experts, methodologists, and other health care personnel
Target audience	Template for application for countries to develop their national approach	Provides specific guidance for the national approach in the United States
Challenges	Must consider developing countries with limited resources and access to asthma specialists	Must consider federal regulations as limitations of recommendations
Revision	Annually	Periodically
Scope	Living document approach that regularly reviews current literature and decides on modifications	Decides which questions to address and then evaluates the literature to make evidence-based recommendations using detailed GRADE methodology
Support system	Previously from restricted education grants from the pharmaceutical industry and now from product sales. Commercial sales allow for widespread advertising with multiple products, such as handbooks, documents, and teaching slides	NIH-directed development and distribution, with limited budget for distribution

GRADE, Grading of Recommendations Assessment, Development and Evaluation; *NIH*, National Institutes of Health.

*This comparison is provided to highlight major differences in approach between the 2 groups of experts that provide direction in asthma care, with specific features to consider in applying their information in clinical practice.

Table IE Implications of strong and conditional recommendations*

Implications	Strong recommendation	Conditional recommendation
For individuals with asthma	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individuals consistent with their values and preferences. Use shared decision making. Decision aids may be useful in helping individuals make decisions consistent with their risks, values, and preferences.
For policymakers	The recommendation can be adapted as policy or performance measure in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Policy making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision making is documented.
For researchers	The recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations.	The recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional (rather than strong) recommendation will help identify possible research gaps.

* **Strong recommendations are indicated by statements that lead with "We recommend," whereas conditional recommendations are indicated by statements that lead with "We conditionally recommend."**

Table 1. Preferred Controller and Reliever Pharmacotherapy Recommendations for Individuals ≥12 Years with Asthma in the NAEPP 2020 Guideline Update and GINA 2020 Report

	NAEPP 2020 Guideline Update	GINA 2020 Report
Step 1	Step 1 therapy not reviewed as part of NAEPP 2020 guideline update	As-needed low-dose ICS-formoterol
Step 2*	Conditional recommendation: Daily low-dose ICS and as-needed SABA or As-needed concomitant low-dose ICS and SABA	Daily low-dose ICS and as-needed SABA or As-needed low-dose ICS-formoterol
Step 3	Strong recommendation: Daily low-dose ICS-formoterol (maintenance and reliever therapy)†	Daily low-dose ICS-LABA and as-needed SABA or Daily low-dose ICS-formoterol (maintenance and reliever therapy)
Step 4	Strong recommendation: Daily medium-dose ICS-formoterol (maintenance and reliever therapy)	Daily medium-dose ICS-LABA and as-needed SABA or Daily medium-dose ICS-formoterol (maintenance and reliever therapy)
Step 5	Conditional recommendation: Daily medium- to high-dose ICS-LABA + LAMA and as-needed SABA	Daily high-dose ICS-LABA and Refer for phenotypic assessment and add-on therapy (e.g., tiotropium, anti-IgE, anti-IL5/5R, and anti-IL4R)
Step 6	Step 6 therapy not reviewed as part of NAEPP 2020 guideline update	Not applicable in GINA

NAEPP 0-4

In children ages 0–4 years with recurrent wheezing triggered by respiratory tract infections and no wheezing between infections, the Expert Panel conditionally recommends:

- starting a short course of daily ICS at the onset of a respiratory tract infection with as-needed SABA for quick-relief therapy compared to as-needed SABA for quick-relief therapy only.

NAEPP AGE 4-11

In individuals ages 4 years and older with mild to moderate persistent asthma who are **likely to be adherent** to daily ICS treatment, the Expert Panel conditionally recommends **against** a short- term increase in the ICS dose for increased symptoms or decreased peak flow.

In individuals ages 4 years and older with moderate to severe persistent asthma, the Expert Panel recommends **ICS-formoterol** in a single inhaler used as both daily controller and reliever therapy **(SMART THERAPY)** compared to either a higher- dose ICS as daily controller therapy and SABA for quick- relief therapy or the same-dose ICS-LABA as daily controller therapy and SABA for quick-relief therapy.

NAEPP AGE 12+

In individuals ages 12 years and older with mild persistent asthma, the Expert Panel conditionally recommends either daily low-dose ICS

and as-needed SABA for quick-relief therapy or as- needed ICS and SABA used concomitantly.

In individuals ages 12 years and older with moderate to severe persistent asthma, the Expert Panel conditionally recommends ICS-formoterol in a single inhaler used as both daily controller and reliever therapy compared to higher-dose ICS-LABA as daily controller therapy and SABA for quick-relief therapy.

CONSIDERATIONS OF SMART (SINGLE MAINTENANCE AND RELIEVER THERAPY)

Maximum number of puffs per day is 8 (36 mcg formoterol) for children ages 4–11 years and 12 (54 mcg formoterol) for individuals ages 12 years and older.

A 1-month supply of ICS-formoterol medication that is sufficient for maintenance therapy may not last a month if the inhaler is used for reliever therapy as well.

LAMA THERAPY

In individuals ages 12 years and older with uncontrolled persistent asthma, the Expert Panel conditionally recommends against adding LAMA to ICS compared to adding LABA to ICS.

If LABA is not used in individuals ages 12 years and older with uncontrolled persistent asthma, the Expert Panel conditionally recommends adding LAMA to ICS controller therapy compared to continuing the same dose of ICS alone.

In individuals ages 12 years and older with uncontrolled persistent asthma, the Expert Panel conditionally recommends adding LAMA to ICS-LABA compared to continuing the same dose of ICS-LABA.

INDOOR ALLERGEN MITIGATION

If indoor allergens found to be contributing to asthma via history or allergy testing, allergen mitigation strategies are recommended. If asthma not allergen related, mitigation strategies are not recommended.

Impermeable pillow/mattress covers are only as part of a multicomponent allergen mitigation intervention, not as a single-component intervention.

Integrated pest management in the home is recommended for individuals with asthma who are allergic and exposed to cockroaches or rodents (e.g., mice)

IMMUNOTHERAPY

In individuals ages 5 years and older with mild to moderate allergic asthma, the Expert Panel conditionally recommends the use of subcutaneous immunotherapy (**SCIT**) as an adjunct treatment to standard pharmacotherapy in those individuals whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy.

In individuals with persistent allergic asthma, the Expert Panel conditionally recommends against the use of sublingual immunotherapy (**SLIT**) in asthma treatment.

FENO

In children ages 0–4 years with recurrent wheezing, the Expert Panel recommends against FeNO measurement to predict the future development of asthma.

In individuals ages 5 years and older for whom the diagnosis of asthma is uncertain using history, clinical findings, clinical course, and spirometry, including bronchodilator responsiveness testing, or in whom spirometry cannot be performed, the Expert Panel conditionally recommends the addition of FeNO measurement as an adjunct to the evaluation process.

FeNO levels greater than 50 ppb (or greater than 35 ppb in children ages 5–12 years) are consistent with elevated T2 inflammation and support a diagnosis of asthma.

FENO CONTINUED

In children ages 0–4 years with recurrent wheezing, the Expert Panel recommends against FeNO measurement to predict the future development of asthma.

In individuals ages 5 years and older for whom the diagnosis of asthma is uncertain using history, clinical findings, clinical course, and spirometry, including bronchodilator responsiveness testing, or in whom spirometry cannot be performed, the Expert Panel conditionally recommends the addition of FeNO measurement as an adjunct to the evaluation process.

BRONCHIAL THERMOPLASTY

In individuals ages 18 years and older with persistent asthma, the Expert Panel conditionally recommends *against* bronchial thermoplasty.

Individuals ages 18 years and older with persistent asthma who place a low value on harms (short- term worsening symptoms and unknown long-term side effects) and a high value on potential benefits (improvement in quality of life, a small reduction in exacerbations) might consider bronchial thermoplasty.

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.			

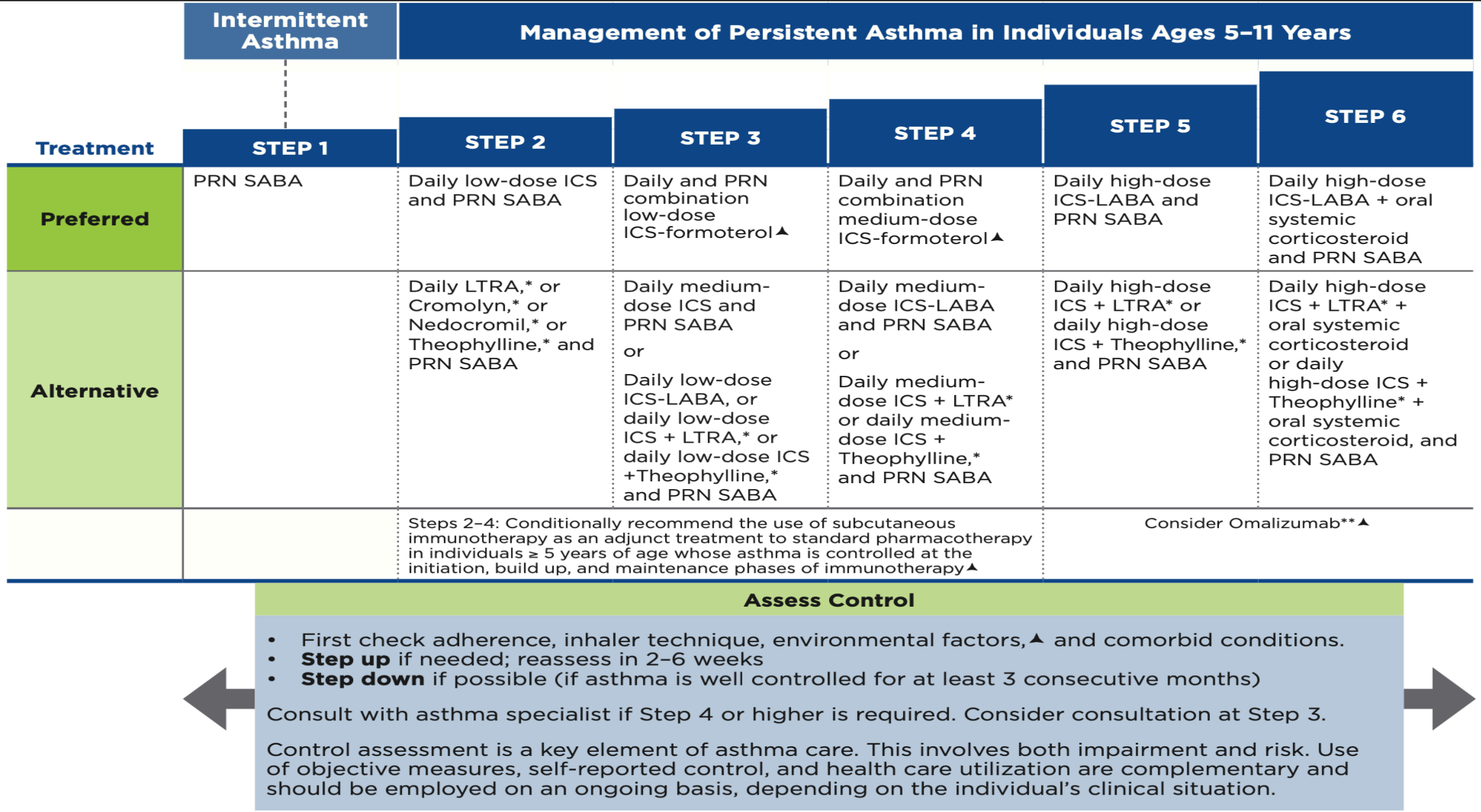
Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 4–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; SABA, inhaled short-acting beta$_2$-agonist; RTI, respiratory tract infection; PRN, as needed



Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	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)**	

THE 12-YEAR HISTORY BEHIND CHANGES IN GINA 2019

Since 2007, GINA has been actively seeking interventions for mild asthma

- to reduce the risk of asthma-related exacerbations and death
- to provide consistent messaging about the goals of asthma treatment, including prevention of exacerbations, across the spectrum of asthma severity
- to avoid establishing patient reliance on SABA early in the course of the disease

GINA emphasized poor adherence as a modifiable risk factor for exacerbations

- When the reliever is SABA, poor adherence with maintenance controller exposes the patient to risks of SABA-only treatment

GINA members repeatedly sought funding for RCTs of as-needed ICS-formoterol for risk reduction in mild asthma

- Eventually culminated in 2014 with the initiation of the SYGMA studies, published in 2018 *(O'Byrne NEJMed 2018; Bateman NEJMed 2018)*

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

This is a population-level risk reduction strategy

- Other examples: statins, anti-hypertensives
- Individual patients may not necessarily experience (or be aware of) short-term clinical benefit
- The aim is to reduce the probability of serious adverse outcomes at a population level

LOW, MEDIUM AND HIGH ICS DOSES: CHILDREN 5 YEARS AND YOUNGER

Inhaled corticosteroid	Low total daily dose (mcg) (age-group with adequate safety and effectiveness data)
BDP (pMDI, standard particle, HFA)	100 (ages 5 years and older)
BDP (pMDI, extrafine particle, HFA)	50 (ages 5 years and older)
Budesonide nebulized	500 (ages 1 year and older)
Fluticasone propionate (pMDI, standard particle, HFA)	50 (ages 4 years and older)
Fluticasone furoate (DPI)	Not sufficiently studied in children 5 years and younger)
Mometasone furoate (pMDI, standard particle, HFA)	100 (ages 5 years and older)
Ciclesonide (pMDI, extrafine particle, HFA)	Not sufficiently studied in children 5 years and younger

This is NOT a table of equivalence. These are suggested total daily doses for the 'low' dose treatment options with different ICS.

BDP: beclometasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC)

ADVERSE EFFECTS WITH MONTELUKAST

FDA boxed warning in March 2020 about risk of serious neuropsychiatric events, including suicidality, with montelukast

- Includes suicidality in adults and adolescents
- Nightmares and behavioral problems in children

Before prescribing montelukast, health professionals should consider its benefits and risks, and patients should be counselled about the risk of neuropsychiatric events

FDA requires Boxed Warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair); advises restricting use for allergic rhinitis

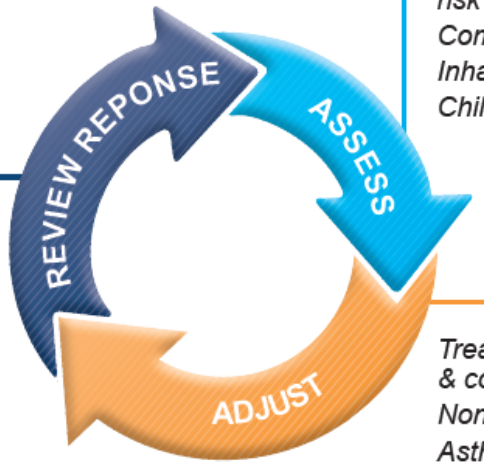
Risks may include suicidal thoughts or actions

Box 3-5B

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review response

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



Symptoms
Exacerbations
Side-effects
Lung function
Child and parent 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

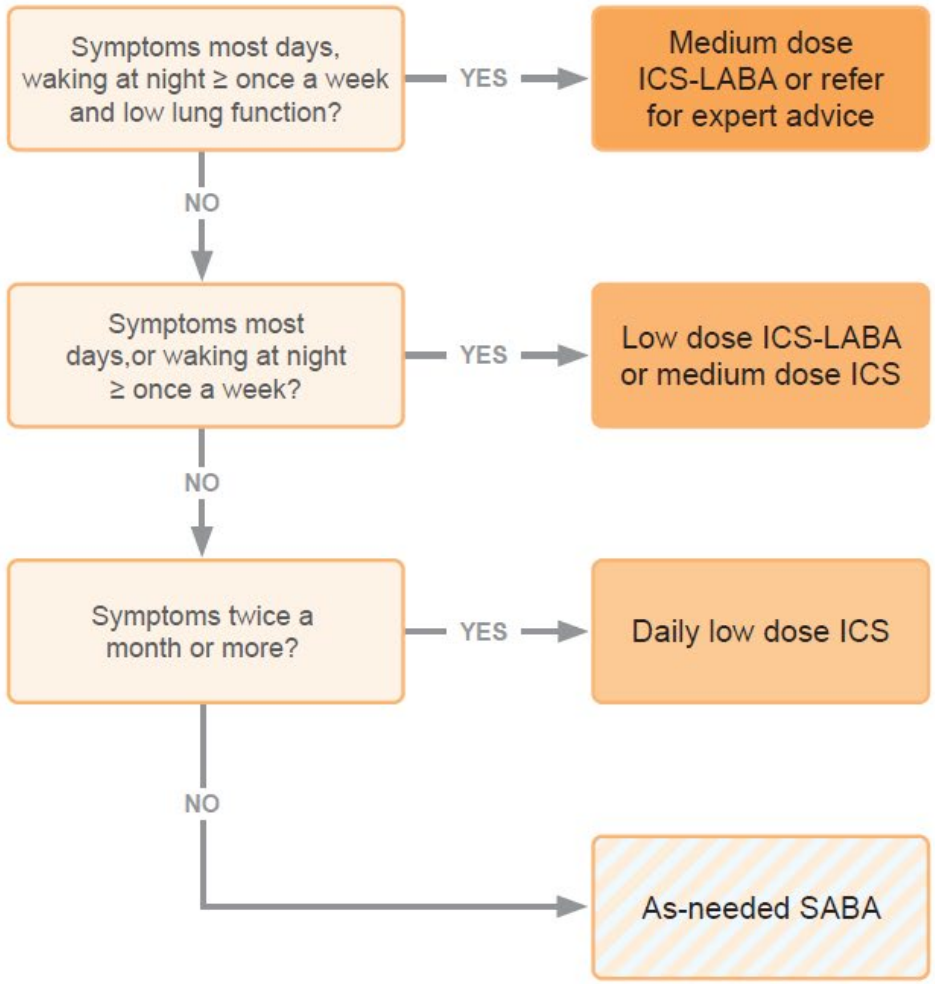
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA or medium dose ICS	Medium dose ICS-LABA Refer for expert advice	Refer for phenotypic assessment ± add-on therapy, e.g. anti-IgE
Other controller options	*Low dose ICS taken whenever SABA taken*; or daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA*	*High dose ICS-LABA, or add-on tiotropium, or add-on LTRA*	*Add-on anti-IL5, or add-on low dose OCS, but consider side-effects*
RELIEVER	*As-needed short-acting β_2-agonist (SABA)*				

* *Separate ICS and SABA inhalers*

SUGGESTED INITIAL CONTROLLER TREATMENT IN CHILDREN 6-11 YEARS WITH A DIAGNOSIS OF ASTHMA

FIRST ASSESS:

- Confirmation of diagnosis
- Symptom control & modifiable risk factors (including lung function)
- Comorbidities
- Inhaler technique & adherence
- Child and parent preferences and goals



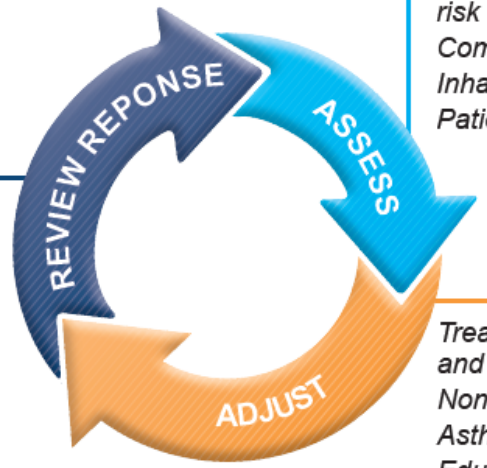
Children 6–11 years

Inhaled corticosteroid	Total daily ICS dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (pMDI, standard particle, HFA)	100–200	>200–400	>400
Beclometasone dipropionate (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, standard particle, HFA)	50-100	>100-200	>200
Mometasone furoate (pMDI, standard particle, HFA)	100		200

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



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

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

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

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	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 Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*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 #*	*Add low dose OCS, but consider side-effects*
PREFERRED RELIEVER	As-needed low dose ICS-formoterol *		As-needed low dose ICS-formoterol for patients prescribed maintenance and reliever therapy‡		
Other reliever option	*As-needed short-acting β_2-agonist (SABA)*				

* *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*

LOW, MEDIUM AND HIGH ICS DOSES: ADULTS/ADOLESCENTS

Adults and adolescents (12 years and older)			
Inhaled corticosteroid	**Total daily ICS dose (mcg)**		
	Low	**Medium**	**High**
Beclometasone dipropionate (pMDI, standard particle, HFA)	200-500	>500-1000	>1000
Beclometasone dipropionate (pMDI, extrafine particle*, HFA)	100–200	>200–400	>400
Budesonide (DPI)	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, standard particle, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	200		400
Mometasone furoate (pMDI, standard particle, HFA)	200-400		>400

This is NOT a table of equivalence. These are suggested total daily doses for the 'low', 'medium' and 'high' dose treatment options with different ICS.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC); * see product information

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities)

6b Consider *add-on biologic Type 2* targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider **local payer eligibility criteria** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Anti-IgE

*Is the patient eligible for **anti-IgE** for severe allergic asthma?*

- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

What factors may predict good asthma response to anti-IgE?

- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no / *no*

Anti-IL5 / Anti-IL5R

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?*

- Exacerbations in last year
- Blood eosinophils ≥300/µl

What factors may predict good asthma response to anti-IL5/5R?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no / *no*

Anti-IL4R

*Is the patient eligible for **anti-IL4R***

… for severe eosinophilic asthma?

- Exacerbations in last year
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

What factors may predict good asthma response to anti-IL4R?

- Higher blood eosinophils +++
- Higher FeNO +++

Anti-IL4R may also be used to treat

- Moderate/severe atopic dermatitis
- Nasal polyposis

Eligible for none?

Return to section **6a**

Choose one if eligible; trial for at least 4 months and assess response

Good asthma response?

yes — Good response to T2-targeted therapy

unclear — Extend trial to 6-12 months

no

STOP add-on

Consider switching to a different Type 2-targeted therapy, if eligible

no — Little/no response to T2-targeted therapy

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