Pharmacotherapy of Asthma: Part 2

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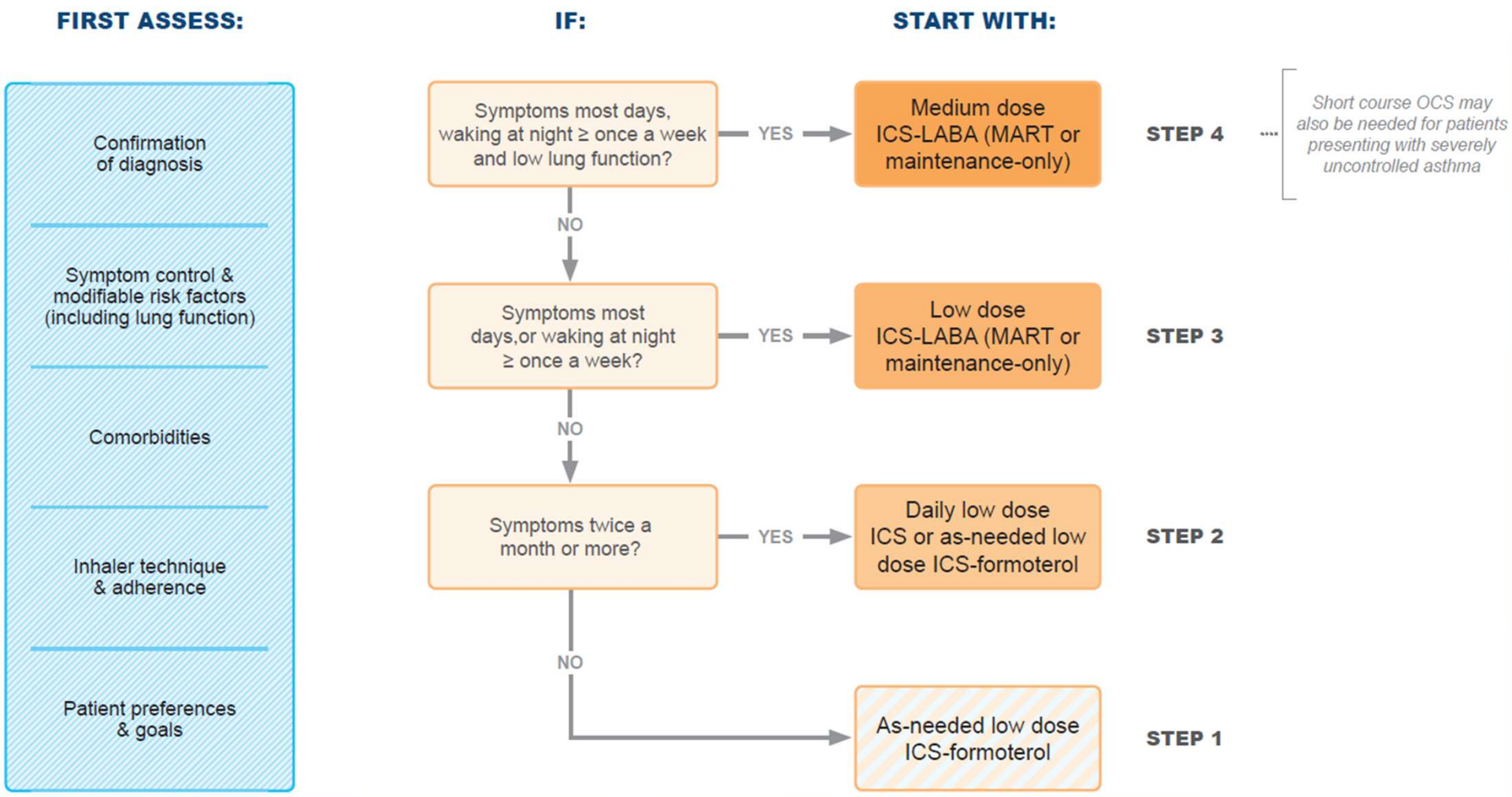
Start ICS-Containing Rx for Adults & Adolescents - GINA 2020

- As soon as possible, after the diagnosis of asthma is made to improve treatment and to reduce risk
  - Patients with even mild asthma can have severe exacerbations
  - Low dose ICS → ↓ hospitalizations & death
  - Low dose ICS → ↓ severe exacs, ↓ Sx, ↑ PFTs, ↓ EIB, even in mild asthma
  - Low dose ICS → ↑ PFTs than if Sx have been present for > 2-4 years
  - Patients not taking ICS who have a severe exac, have ↓ long-term lung function than those who have started ICS
  - In occupational asthma, early removal from exposure & early Rx increase chance of recovery
- Most patients with asthma do not need more than low dose ICS

SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA



GINA 2020, Box 3-4B

NAEPP Expert Panel 2020 Focused Asthma Updates

- 6 priority topics for priority review, incduing intermittent ICSs and role of LAMAs
- Cromolyn, nedocromil, LTRAs, and theophylline were not included, due to less desirability
  - Limited availability *and/or*
  - Increased risk of adverse events *and/or*
  - Need for monitoring

J Allergy Immunol 2020;146:1217-70

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)**	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

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.

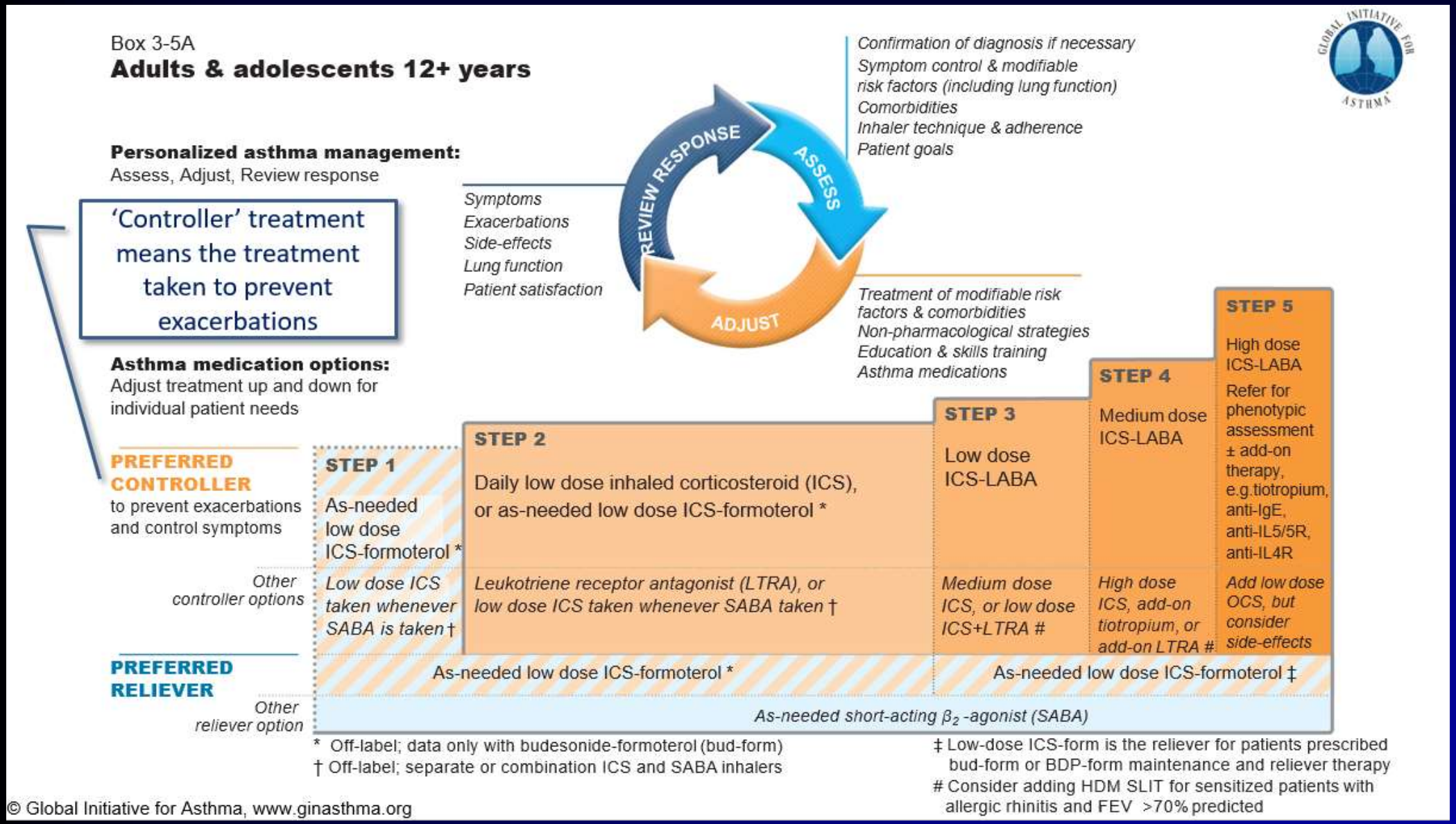
J Allergy Clin Immunol 2020;146:1217-70

NOTES FOR INDIVIDUALS AGES 12+ YEARS DIAGRAM

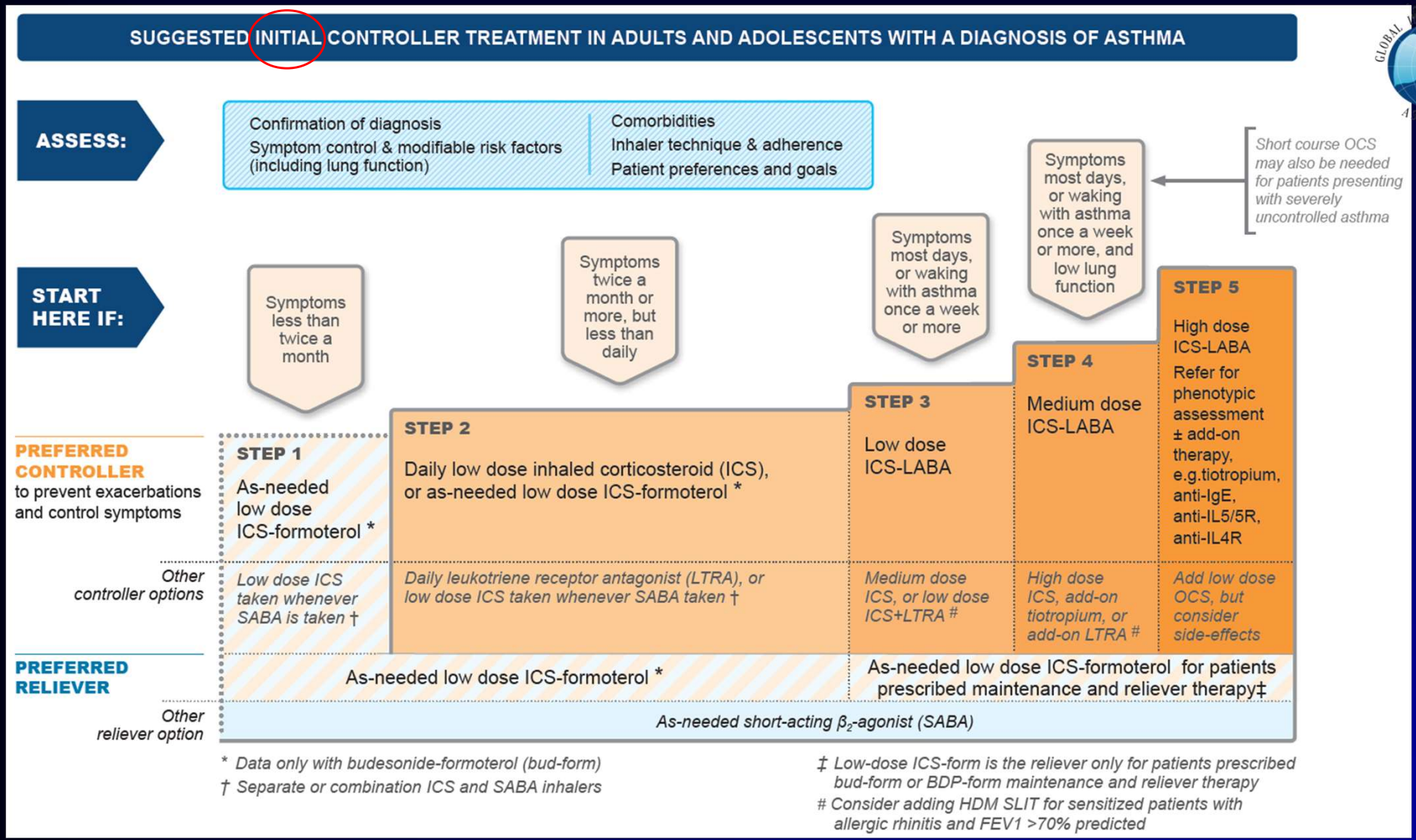
Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on the severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • In steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 12 puffs (54 mcg).▲ • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• The terms ICS-LABA and ICS-formoterol indicate combination therapy with both an ICS and a LABA, usually and preferably in a single inhaler. • Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol. • In individuals ages 12 years and older with persistent allergic asthma in which there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessment. • Bronchial thermoplasty was evaluated in Step 6. The outcome was a conditional recommendation against the therapy.

J Allergy Clin Immunol 2020;146:1217-70

GINA 2020



*Step 2 – Daily LTRA



GINA 2020, Box 7B

Step 1
Adults & Adolescents

NAEPP

- Preferred
  - prn SABA

GINA

- Preferred Controller
  - prn low-dose ICS/formoterol
- Other options
  - Low dose ICS whenever SABA taken
- Preferred Reliever
  - prn low-dose ICS/formoterol
  - Other option: prn SABA

GINA 2019/2020: Step 1

- For safety, GINA no longer recommends **prn SABA alone**
  - Does not protect from severe exacerbations.
  - Regular or frequent use of SABAs ↑ risk of exacerbations.
- New controller options for adults & adolescent (Sx < 2x/month & no exacerbation risk factors)
  - prn low-dose ICS-formoterol*
  - **OR** IF NOT AVAILABLE, low-dose ICS taken whenever SABA is taken*

*off-label, all evidence with budesonide/formoterol

www.ginasthma.org

Step 2
Adults and Adolescents

NAEPP

- Preferred controller
  - Daily low dose ICS & prn SABA
  - prn concomitant ICS/SABA
- Other options
  - Daily LTRA & prn SABA
  - Cromolyn or nedocromil or theophylline & prn SABA
- Steps 2-4: consider immunotherapy when warranted

GINA

- Preferred controller
  - Daily low dose ICS
  - prn low dose ICS/formoterol
- Other options
  - Daily LTRA
  - Low dose ICS taken whenever SABA is taken

GINA 2019/2020: Step 2

- Two "preferred" controller options
  - Regular low-dose ICS
  - As-needed low-dose ICS – formoterol*
- Other controller options
  - Low-dose ICS taken whenever SABA taken* (*off-label, as separate or combination inhalers)
  - Daily leukotriene receptor antagonist (LTRA) **(LESS EFFECTIVE FOR EXACERBATIONS)**
- Preferred reliever – prn low dose ICS/formoterol*
- All steps: prn SABA is "Other reliever option"

www.ginasthma.org

Step 3
Adults & Adolescents

NAEPP

- Preferred controller
  - Daily **AND** prn low dose combination ICS/formoterol*
- Other options (& prn SABA)
  - Daily medium dose ICS Daily low dose ICS/LABA
  - Daily low dose ICS/LAMA
  - Daily low dose ICS/LTRA
  - Daily low dose ICS/theophylline

GINA

- Preferred controller
  - Daily low dose ICS/LABA **AND** prn low dose combination ICS/formoterol*
- Other options
  - Medium dose ICS
  - Low dose ICS/LTRA

GINA 2019/2020: Step 3

- Before step-up, check diagnosis, inhaler technique, adherence, & co-morbidity
- Preferred controller option
  - Low-dose ICS-LABA maintenance
- Other options
  - Medium-dose ICS
  - Low-dose ICS plus LTRA
  - For adults with rhinitis who are allergic to house dust mite, consider adding sublingual immunotherapy (SLIT), if FEV_1>70% predicted
- Preferred reliever – prn low dose ICS/formoterol*, for patients prescribed maintenance and reliever therapy

Step 4
Adults & Adolescents

NAEPP

- Preferred Controller
  - Daily **and** prn combination medium dose ICS/formotorol
- Other options (& prn SABA)
  - Medium dose ICS/LABA
  - Medium dose ICS/LAMA
  - Medium dose ICS/LTRA
  - Medium dose ICS/ theophylline

GINA

- Preferred controller
  - Medium dose ICS/LABA
- Other options
  - High dose ICS with add-on:
    - Tiotropium
    - LTRA

GINA 2019/2020: Step 4

- Before step-up, check inhaler technique & adherence
- Preferred controller option
  - Medium-dose ICS-LABA maintenance
- Other options
  - High dose ICS
  - Add-on tiotropium by mist inhaler
  - Add-on LTRA
  - SLIT if house dust allergic, and if FEV_1 > 70%
- Preferred reliever – prn low dose ICS/formoterol* for patients prescribed maintenance and reliever therapy

Step 5
Adults & Adolescents

NAEPP

- Preferred controller
  - Medium-high dose ICS/LABA/LAMA
- Alternate controller
  - Medium-high dose ICS/LABA
  - High dose ICS/LTRA
- Consider add-on therapy with biologics

GINA

- Preferred controller
  - High dose ICS/LABA
  - Phenotypic assessment
  - Add-on therapy
    - Tiotropium
    - Anti-IgE
    - Anti-IL5/5R
    - Anti-IL4R
- Alternate controller
  - Add low dose OCS
    - Consider side-effects

GINA 2019/2020: Step 5

- In patients with uncontrolled Sx &/or exacerbations despite Step 4,
  - High-dose ICS-LABA
    - assess for contributory factors, optimal treatment, & refer for expert asthma assessment, including severe asthma phenotype, & potential add-on Tx
- Potential add-on treatments
  - Tiotropium
  - Biologics (based on phenotype)
    - Anti-IgE (omalizumab), anti-IL5/5R (mepolizumab, reslizumab, benralizumab), anti IL4R (dupilumab)
- Other options: low-dose OCS (systemic side effects)
- Preferred reliever – prn low dose ICS/formoterol* for patients prescribed maintenance and reliever therapy

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

GINA 2020, Box 3-6A

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

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
	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**▲	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

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.

J Allergy Clin Immunol 2020;146:1217-70

NOTES FOR INDIVIDUALS AGES 5–11 YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • In Steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 8 puffs (36 mcg).▲ • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• The terms ICS-LABA and ICS-formoterol indicate combination therapy with both an ICS and a LABA, usually and preferably in a single inhaler. • Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol. • In individuals ages 5–11 years with persistent allergic asthma in which there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessment.

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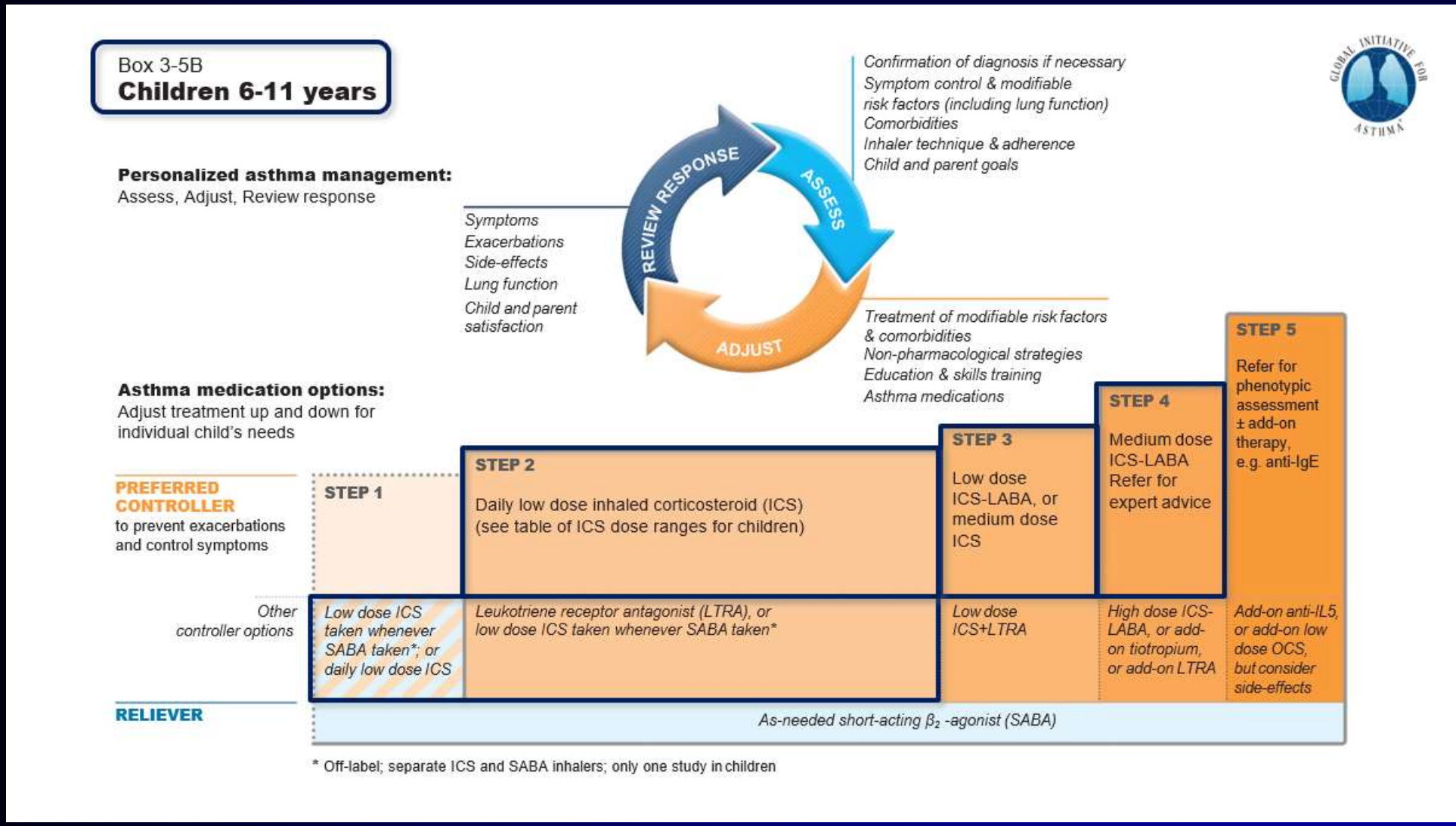
GINA 2020: Children 6-11



NAEPP/GINA: Step 1
Children 5 to 6-11 years

- Indication: symptoms < 2/month
- Preferred options
  - prn SABA (preferred reliever for all Steps)
- Other options
  - Low dose ICS taken whenever SABA used (consider likelihood of appropriate adherence)
  - Daily low dose ICS

GINA 2020 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

NAEPP/GINA: Step 2 Children 5 to 6 – 11 years

- Indication: symptoms ≥ 2/month, but < daily
- Preferred options:
  - Low dose ICS and prn SABA
- Other options:
  - LTRA or theophylline and prn SABA
  - Low dose ICS concomitantly with prn SABA
  - Conditional recommendation of subQ immunotherapy
  - Studies of as-needed ICS-formoterol are needed; maintenance and reliever therapy with low dose budesonide-formoterol in children 4-11 years reduced exacerbations by 70-79% compared with ICS and ICS-LABA *(Bisgaard, Chest 2006)*

GINA 2020 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

NAEPP/GINA: Step 3
Children 5 to 6 – 11 years

- Indication: symptoms most days, waking with asthma ≥ 1/week
- Preferred options
  - Low dose ICS/LABA and prn SABA
  - Daily **and** prn low dose ICS/formoterol*
- Other options
  - Low dose ICS/LTRA or theophylline
  - Medium dose ICS
  - Conditional recommendation of subQ immunotherapy
  - No safety signal with ICS-LABA in children 4-11 years *(Stempel, NEJMed 2017)*

GINA 2020 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

NAEPP/GINA: Step 4
Children 5 to 6 – 11 years

- Indication: symptoms most days, waking with asthma ≥ 1/week, and low lung function
- Preferred options:
  - Medium dose ICS/LABA, refer to specialist
  - Daily **and** prn medium dose ICS/formoterol*
- Other options:
  - Medium dose ICS/LTRA or theophylline
  - High dose ICS/LABA
  - Add-on tiotropium or add-on LTRA
  - Conditional recommendation of subQ immunotherapy
  - Short course OCS may be indicated

GINA 2020 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

NAEPP/GINA: Step 5
Children 5 to 6 – 11 years

- Preferred options:
  - Continue Step 4 and refer for phenotypic assessment & add-on therapy (e.g. anti-IgE)
  - High dose ICS/LABA
- Other options:
  - High dose ICS/LTRA or theophylline
  - Add-on anti-IL5
  - Add-on low dose OCS (consider side effects)

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J Allergy Clin Immunol 2020:146:2017-70

NAEPP: Step 6
Children 5 – 11 years

- Preferred option:
  - High dose ICS/LABA & oral OCS
- Other options:
  - High dose ICS/LTRA or theophylline with OCS
  - Consider anti-IgE (omalizumab)

GINA 2020 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

GINA 2020: Children 6-11

- **Preferred reliever for all steps: prn SABA**
- Step 1
  - Low dose ICS taken whenever SABA is taken (consider likelihood of good adherence)
  - Daily low dose ICS
- Step 2
  - Daily low dose ICS
  - Daily LTRA or low dose ICS taken whenever SABA is taken
  - Studies of as-needed ICS-formoterol are needed; maintenance and reliever therapy with low dose budesonide-formoterol in children 4-11 years reduced exacerbations by 70-79% compared with ICS and ICS-LABA *(Bisgaard, Chest 2006)*

Low, medium and high ICS doses: children 6-11 years

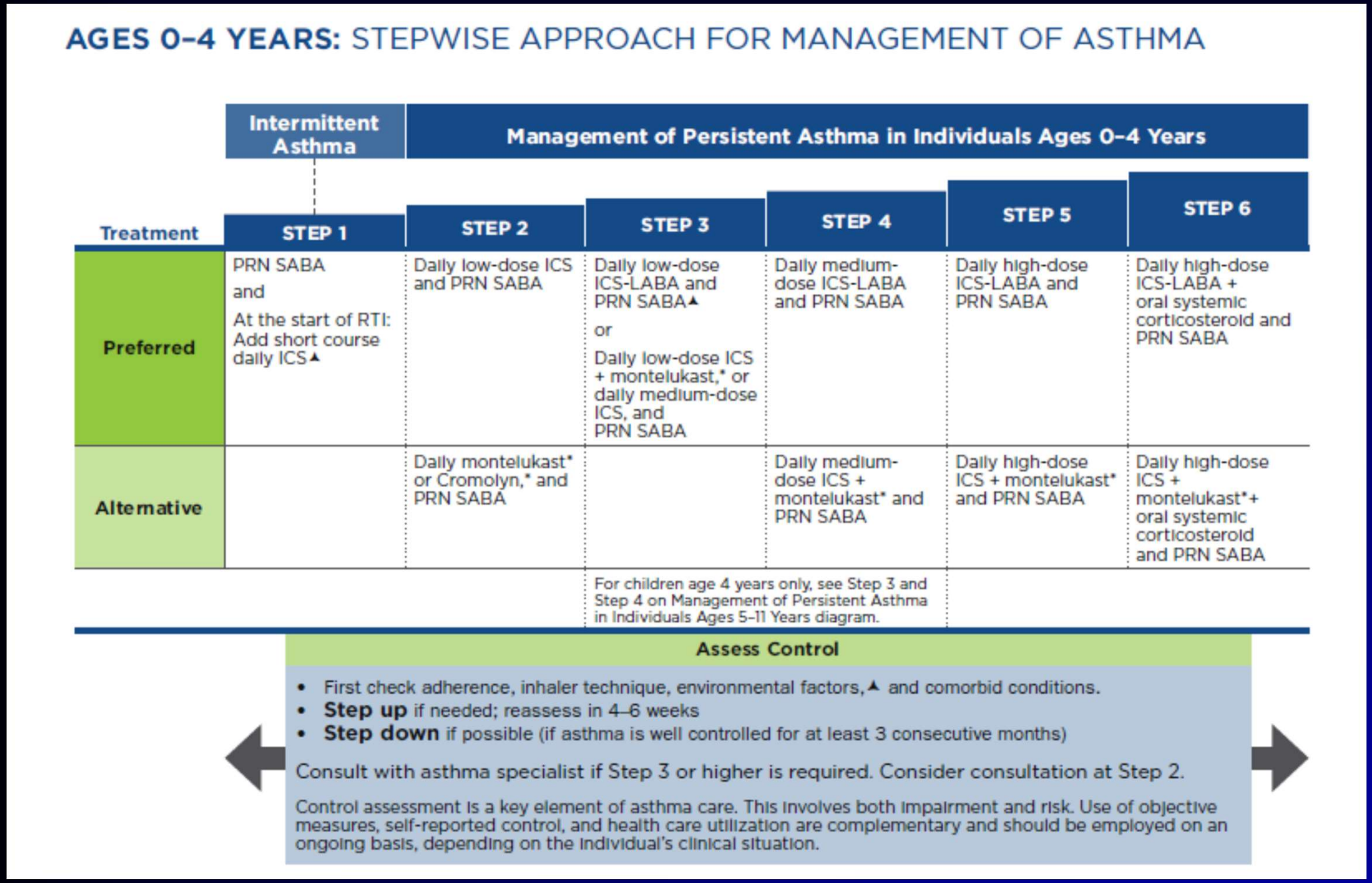
Children 6–11 years			
Inhaled corticosteroid	Total daily ICS dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (pMDI, standard particle, HFA)	100–200	>200–400	>400
Beclometasone dipropionate (pMDI, extrafine particle*, HFA)	50-100	>100-200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (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

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

GINA 2020, Box 3-6B

NAEPP Expert Panel 2020



J Allergy Clin Immunol 2020;146:1217-70

NOTES FOR INDIVIDUALS AGES 0–4 YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment. • Consider short course of oral systemic corticosteroid if exacerbation is severe or individual has history of previous severe exacerbations.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• If clear benefit is not observed within 4–6 weeks and the medication technique and adherence are satisfactory, the clinician should consider adjusting therapy or alternative diagnoses.

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Intermittent ICS Recommendations

- Children ages 0-4
  - ≥ 3 wheezing episodes triggered by URI during lifetime OR ≥ 2 simililar wheezing episodes in the past year AND asymptomatic between periods of URI
  - 7-10 day course of ICS with prn SABA starting at onset of signs/symptoms of URI

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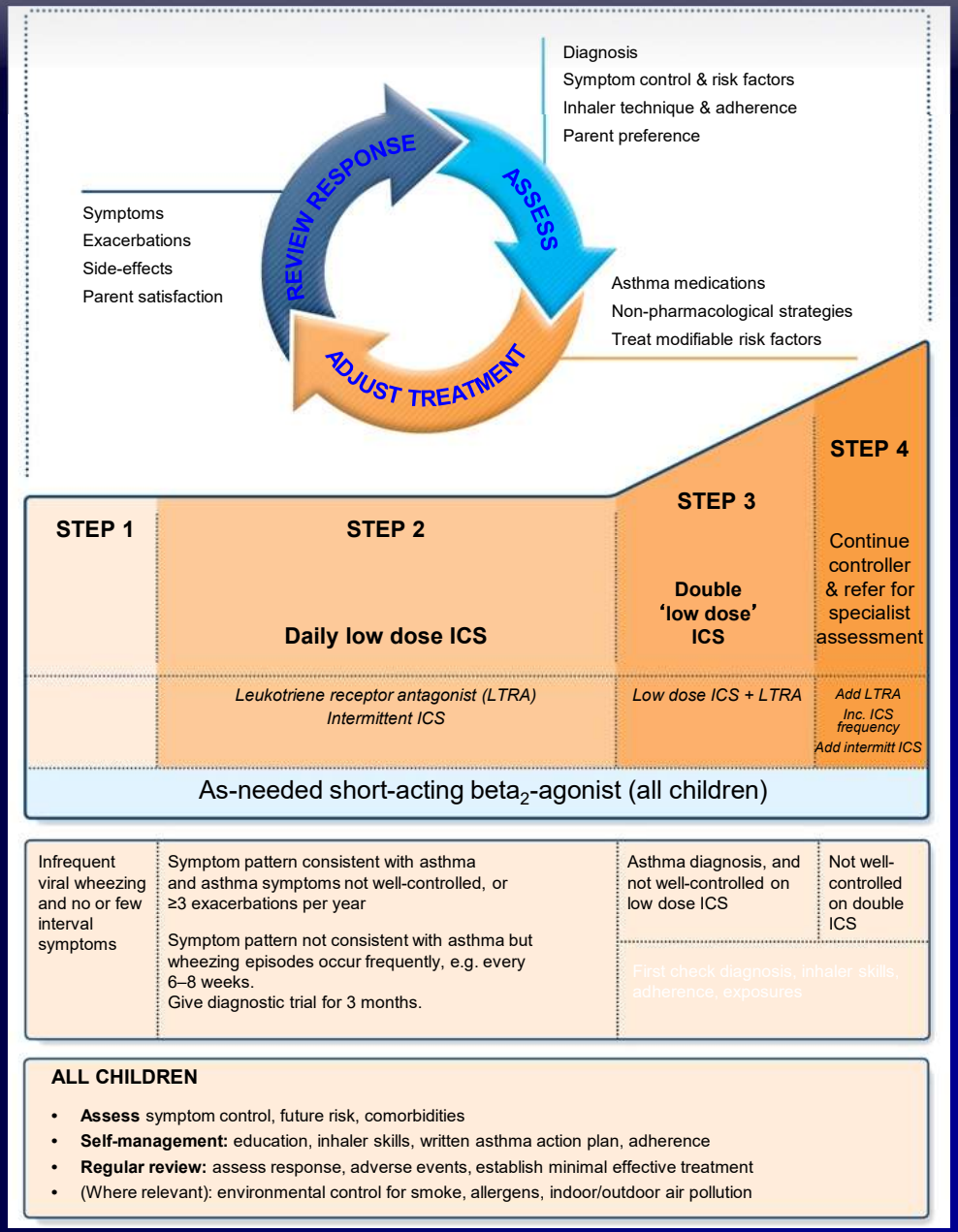
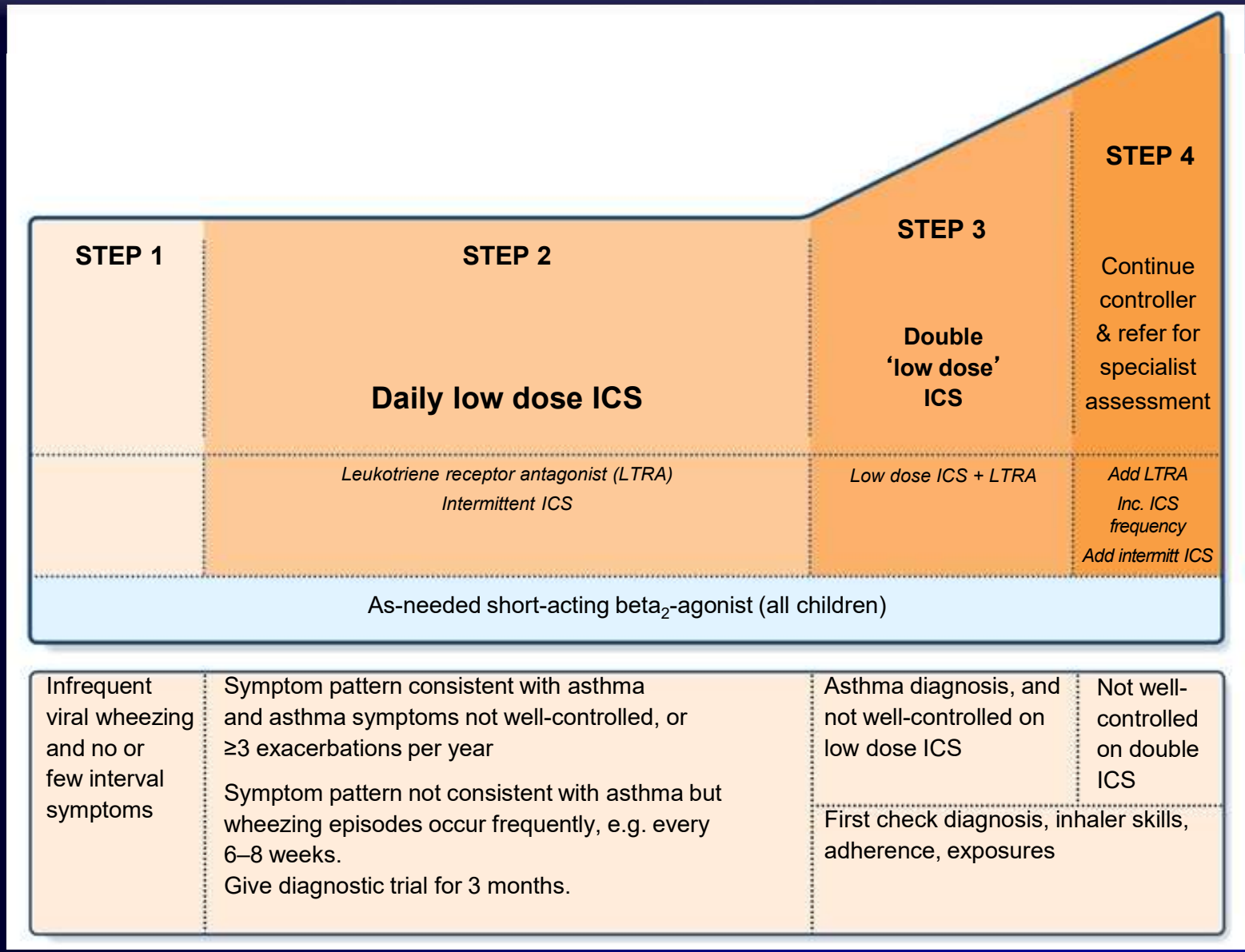
Stepwise approach to control symptoms and reduce risk (children ≤5 years)



GINA 2017, Box 6-5 (2/8)

Stepwise approach – pharmacotherapy (children ≤5 years)



GINA 2017, Box 6-5 (3/8)

Stepwise approach – key issues (children ≤5 years)

UPDATED 2017

KEY ISSUES

ALL CHILDREN

- **Assess** symptom control, future risk, comorbidities
- **Self-management:** education, inhaler skills, written asthma action plan, adherence
- **Regular review:** assess response, adverse events, establish minimal effective treatment
- (Where relevant): environmental control for smoke, allergens, indoor/outdoor air pollution

- Assess asthma control
  - Symptom control, future risk, comorbidities
- Self-management
  - Education, inhaler skills, written asthma action plan, adherence
- Regular review
  - Assess response, adverse events, establish minimal effective treatment
  - Record height each year, as poorly-controlled asthma may influence growth, and ICS may be associated with growth delay in first 1-2 years
- Other
  - (Where relevant): environmental control for smoke, allergens, indoor or outdoor air pollution

GINA 2017, Box 6-5 (4/8)

NAEPP: Step 1
Children 0-4 years

- Preferred option: as-needed inhaled SABA
  - Provide inhaled SABA to all children who experience wheezing episodes
  - Add short course daily ICS at start of viral induced illness (consider likelihood of appropriate adherence)
- Other options
  - Oral bronchodilator therapy is not recommended (slower onset of action, more side-effects)

J Allergy Clin Immunol.2020

NAEPP/GINA: Step 2
Children 0-4 years

- Indication
  - Child with symptom pattern consistent with asthma, and symptoms not well-controlled, or ≥3 exacerbations per year
  - May also be used as a diagnostic trial for children with frequent wheezing episodes
- Preferred option: regular daily low dose ICS + as-needed inhaled SABA
  - Give for 4-6 weeks to establish effectiveness, and review response
- Other options depend on symptom pattern
  - (Persistent asthma) – regular leukotriene receptor antagonist (LTRA) leads to modest reduction in symptoms and need for OCS compared with placebo
  - (Frequent viral-induced wheeze with interval symptoms) – consider episodic or as-needed ICS, but give a trial of regular ICS first

GINA 2017 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

NAEPP/GINA Step 3: Children 0-4 years

- Indication
  - Asthma diagnosis, and symptoms not well-controlled on low dose ICS
  - Evaluate diagnosis, adherence, inhaler technique and environmental exposures
- Preferred option:
  - Medium dose ICS and prn SABA
  - Low dose ICS/LABA and prn SABA
  - Reassess in 4-6 weeks
- Other options
  - Consider adding LTRA to low dose ICS

GINA 2017 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

NAEPP/GINA: Step 4 Children 0-4 years

- Indication:
  - Not well controlled on Step 3 therapy
  - Evaluate diagnosis, adherence, inhaler technique, environmental exposures
- Preferred options:
  - Continue current controller & refer to specialist
  - Medium dose ICS/LABA and prn SABA
  - Reevaluate in 4-6 weeks
- Other options
  - Add LTRA, ↑ICS dose/frequency, add intermittent ICS
  - Medium dose ICS/LTRA and prn SABA
  - NAEPP: children age ≥ 4 years may use guildelines for ages 5-11

GINA 2017 www.ginaasthma.org
J Allergy Clin Immunol 2020:146:2017-70

'Low dose' inhaled corticosteroids (mcg/day) for children ≤5 years

Inhaled corticosteroid	Low daily dose (mcg)
Beclometasone dipropionate (HFA)	100
Budesonide (pMDI + spacer)	200
Budesonide (nebulizer)	500
Fluticasone propionate (HFA)	100
Ciclesonide	160
Mometasone furoate	Not studied below age 4 years
Triamcinolone acetonide	Not studied in this age group

- This is not a table of equivalence
- A low daily dose is defined as the dose that has not been associated with clinically adverse effects in trials that included measures of safety

GINA 2017, Box 6-6

Checking height in children with asthma

NEW 2017

- Check height at least yearly, because:
  - Poorly-controlled asthma can affect growth *[Pedersen 2001]*
  - Growth velocity may be lower in the first 1-2 years of ICS treatment but this is not progressive or cumulative *[Kelly 2012, Loke 2015]*.
  - The one study that examined long-term outcomes showed a difference of only 0.7% in adult height *[Kelly 2012, Loke 2015]*
- If decreased growth velocity is seen, also consider:
  - Poorly-controlled asthma
  - Frequent use of OCS
  - Poor nutrition

Inhaled corticosteroids and growth in children

NEW SLIDE 2017

- **Discuss decisions about controller treatment with parents/carers**
  - Discuss the relative benefits and risks of treatment/no treatment
  - Emphasize the importance of maintaining normal activity levels for normal physical and social development
- **ICS can have a small but usually temporary effect on growth**
  - An effect of ICS on growth velocity is seen in pre-pubertal children in the first 1-2 years of treatment
  - This is <u>not</u> progressive or cumulative *[Kelly 2012, Loke 2015]*.
  - The one study that examined long-term outcomes showed a difference of only 0.7% in adult height *[Kelly 2012, Loke 2015]*
- **Poorly-controlled asthma itself adversely affects adult height** ***[Pedersen 2001]***

Reviewing response and adjusting treatment

- How often should asthma be reviewed?
  - 1-3 months after treatment started, then every 3-12 months
  - During pregnancy, every 4-6 weeks
  - After an exacerbation, within 1 week
- Stepping up asthma treatment
  - *Sustained step-up*, for at least 2-3 months if asthma poorly controlled
    - Important: first check for common causes (symptoms not due to asthma, incorrect inhaler technique, poor adherence)
  - *Short-term step-up*, for 1-2 weeks, e.g. with viral infection or allergen
    - May be initiated by patient with written asthma action plan
  - *Day-to-day adjustment*
    - For patients prescribed low-dose ICS/formoterol maintenance and reliever regimen*
- Stepping down asthma treatment
  - Consider step-down after good control maintained for 3 months
  - Find each patient's minimum effective dose, that controls both symptoms and exacerbations

*Approved only for low dose beclometasone/formoterol and low dose budesonide/formoterol

GINA 2019

General principles for stepping down controller treatment

- Aim
  - To find the lowest dose that controls symptoms and exacerbations, and minimizes the risk of side-effects
- When to consider stepping down
  - When symptoms have been well controlled and lung function stable for ≥3 months
  - No respiratory infection, patient not travelling, not pregnant
- Prepare for step-down
  - Record the level of symptom control and consider risk factors
  - Make sure the patient has a written asthma action plan
  - Book a follow-up visit in 1-3 months
- Step down through available formulations
  - Stepping down ICS doses by 25–50% at 3 month intervals is feasible and safe for most patients *(Hagan et al, Allergy 2014)*
  - See GINA 2017 report Box 3-7 for specific step-down options
- Stopping ICS is not recommended in adults with asthma because of risk of exacerbations *(Rank et al, JACI 2013)*

Preferred controller/reliever recommendations

	NAEPP 2020	GINA 2020
Step 1	Not reviewed	prn low-dose ICS/formoterol
Step 2	Daily low-dose ICS & prn SABA **or** prn low-dose ICS with SABA	Daily low-dose ICS & prn SABA **or** prn low-dose ICS/formoterol
Step 3	Daily low-dose ICS/formoterol (Maintenance & reliever therapy)	Daily low-dose ICS/LABA & prn SABA **or** Daily low-dose ICS/formoterol as maintenance & reliever therapy
Step 4	Daily medium-dose ICS/formoterol (Maintenance & reliever therapy)	Daily medium-dose ICS/formoterol & prn SABA **or** Daily medium-dose ICS/formoterol (Maintenance & reliever therapy)
Step 5	Daily medium-high dose ICS/LABA/LAMA& prn SABA	Daily high-dose ICS/LABA Phenotypic add on tx: tiotropium, biologics
Step 6	Not reviewed	Not applicable

AJRCCM in press. Published 12/3/2020 as10.1164/rccm.202011-4236ED

Intermittent ICS

- Scheduled, daily ICS treatment is currently the preferred controller therapy for persistent asthma in individuals of all ages
- Intermittent = courses of ICS therapy used for brief periods (in response to symptoms or as add-on therapy)

J Allergy Clin Immunol 2020;146:1217-70

Intermittent ICS Recommendations

- Individuals ≥ 12 years with mild persistent asthma, use either
  - Daily low-dose ICS and prn SABA
    - For patients who are under or over perceivers of their asthma symptoms
  - prn ICS with SABA used concomitantly
    - 2-4 puffs of SABA with low-dose ICS q4h prn
- Regular follow up recommended to determine appropriateness of regimen

J Allergy Clin Immunol 2020;146:1217-70

Intermittent ICS Recommendations

- In individuals ≥ 4 years with moderate-severe persistent asthma, ICS-formoterol in a single inhaler may be used as **both** daily controller therapy **and** reliever therapy compared to daily high-dose ICS and prn SABA or daily ICS/LABA and prn SABA
  - Maximum daily formoterol dose
    - 36 mcg for ages 4-11
    - 54 mcg for ages ≥ 12 years

J Allergy Clin Immunol 2020;146:1217-70

Intermittent ICS Recommendations

- In individuals ≥ 4 years with moderate-severe persistent asthma
  - May not be necessary for patients whose asthma is currently well controlled using alternate regiments
  - Appropriate for Step 3 & Step 4 treatment
  - This therapy should not be used in patients using ICS/salmeterol maintenance
  - Administer as ICS/formoterol maintenance as 1-2 puffs 1-2 times daily and 1-2 puffs prn

J Allergy Clin Immunol 2020;146:1217-70

COVID-19 and asthma *(as at April 3, 2020)*

- Advise patients with asthma to continue taking their prescribed asthma medications, particularly *inhaled corticosteroids* (ICS), and oral corticosteroids (OCS) if prescribed
  - Asthma medications should be continued as usual. Stopping ICS often leads to potentially dangerous worsening of asthma
  - For patients with severe asthma: continue biologic therapy, and do not suddenly stop OCS if prescribed
- Make sure that all patients have a *written asthma action plan* with instructions about:
  - Increasing controller and reliever medication when asthma worsens
  - Taking a short course of OCS for severe asthma exacerbations
  - When to seek medical help
  - See the GINA 2020 report for more information about treatment options for asthma action plans.
- *Avoid nebulizers* where possible
  - Nebulizers increase the risk of disseminating virus to other patients AND to health care professionals
  - Pressurized metered dose inhaler via a spacer is the preferred treatment during severe exacerbations, with a mouthpiece or tightly fitting face mask if required

GINA 2020

COVID-19 and asthma

(as at March 30, 2020)

- *Avoid spirometry* in patients with confirmed/suspected COVID-19
  - Spirometry can disseminate viral particles and expose staff and patients to risk of infection
  - While community transmission of the virus is occurring in your region, postpone spirometry and peak flow measurement within health care facilities unless there is an urgent need
  - Follow contact and droplet precautions
- *Follow strict infection control procedures* if aerosol-generating procedures are needed
  - For example: nebulization, oxygen therapy (including with nasal prongs), sputum induction, manual ventilation, non-invasive ventilation and intubation
  - World Health Organization (WHO) infection control recommendations are found here: www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125
- *Follow local health advice* about hygiene strategies and use of personal protective equipment, as new information becomes available in your country or region