Asthma

What is new in diagnosis and treatment 2020

H.Esmaeilzadeh,MD

Associate prof. of Allergy and Clinical immunology, Shiraz university of medical sciences

Global Initiative for Asthma (GINA)

What's new in GINA 2020?

GINA Global Strategy for Asthma Management and Prevention

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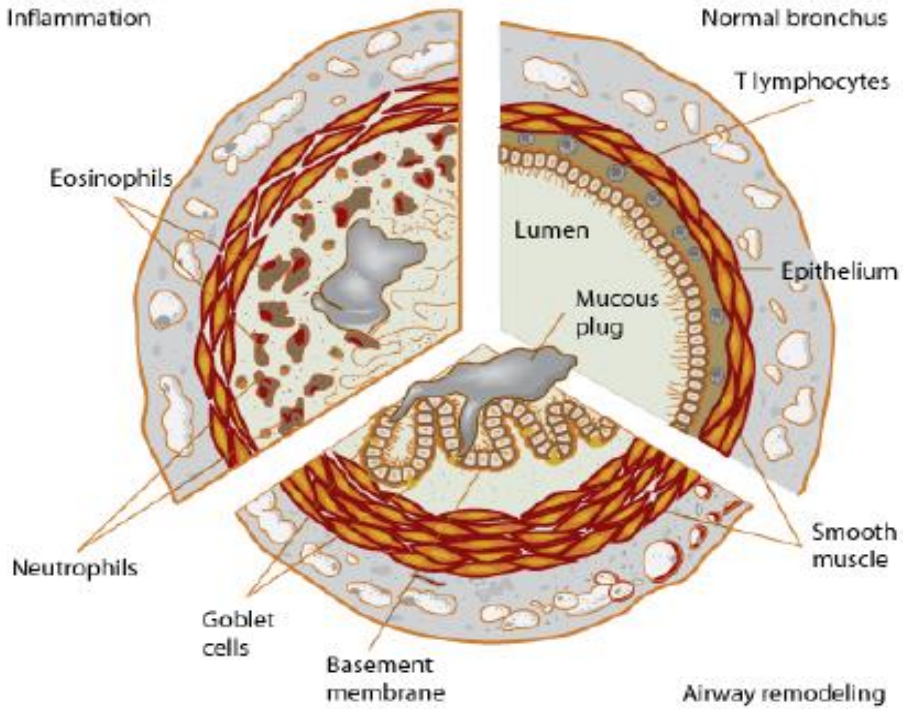
Definition of asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.

It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

Pathophysiology



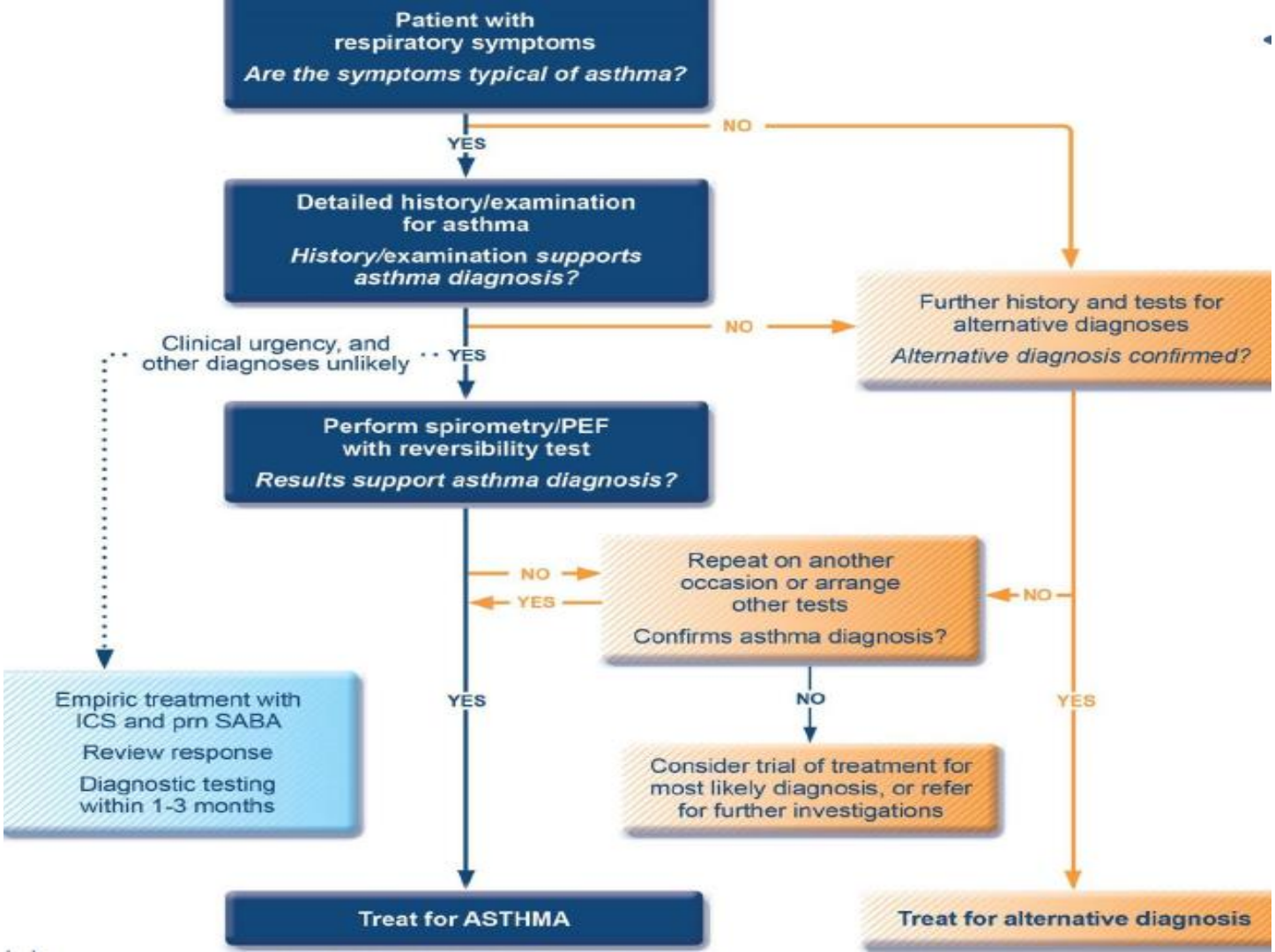
Source: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: *Pharmacotherapy: A Pathophysiologic Approach, 8th Edition*: www.accesspharmacy.com

Diagnosis of asthma – symptoms

- *Increased* probability that symptoms are due to asthma if:
  - More than one type of symptom (wheeze, shortness of breath, cough, chest tightness)
  - Symptoms often worse at night or in the early morning
  - Symptoms vary over time and in intensity
  - Symptoms are triggered by viral infections, exercise, allergen exposure, changes in weather, laughter, irritants such as car exhaust fumes, smoke, or strong smells
- *Decreased* probability that symptoms are due to asthma if:
  - Isolated cough with no other respiratory symptoms
  - Chronic production of sputum
  - Shortness of breath associated with dizziness, light-headedness or peripheral tingling
  - Chest pain
  - Exercise-induced dyspnea with noisy inspiration (stridor)

Diagnosis of asthma – variable airflow limitation

- Confirm presence of airflow limitation
  - Document that FEV_1/FVC is reduced (at least once, when FEV_1 is low)
  - FEV_1/ FVC ratio is normally >0.75 – 0.80 in healthy adults, and >0.90 in children
- Confirm variation in lung function is greater than in healthy individuals
  - The greater the variation, or the more times variation is seen, the greater probability that the diagnosis is asthma
  - Excessive bronchodilator reversibility (adults: increase in FEV_1 >12% and >200mL; children: increase >12% predicted)
  - Excessive diurnal variability from 1-2 weeks' twice-daily PEF monitoring (daily amplitude x 100/daily mean, averaged)
  - Significant increase in FEV_1 or PEF after 4 weeks of controller treatment
  - If initial testing is negative:
    - Repeat when patient is symptomatic, or after withholding bronchodilators
    - Refer for additional tests (especially children ≤5 years, or the elderly)

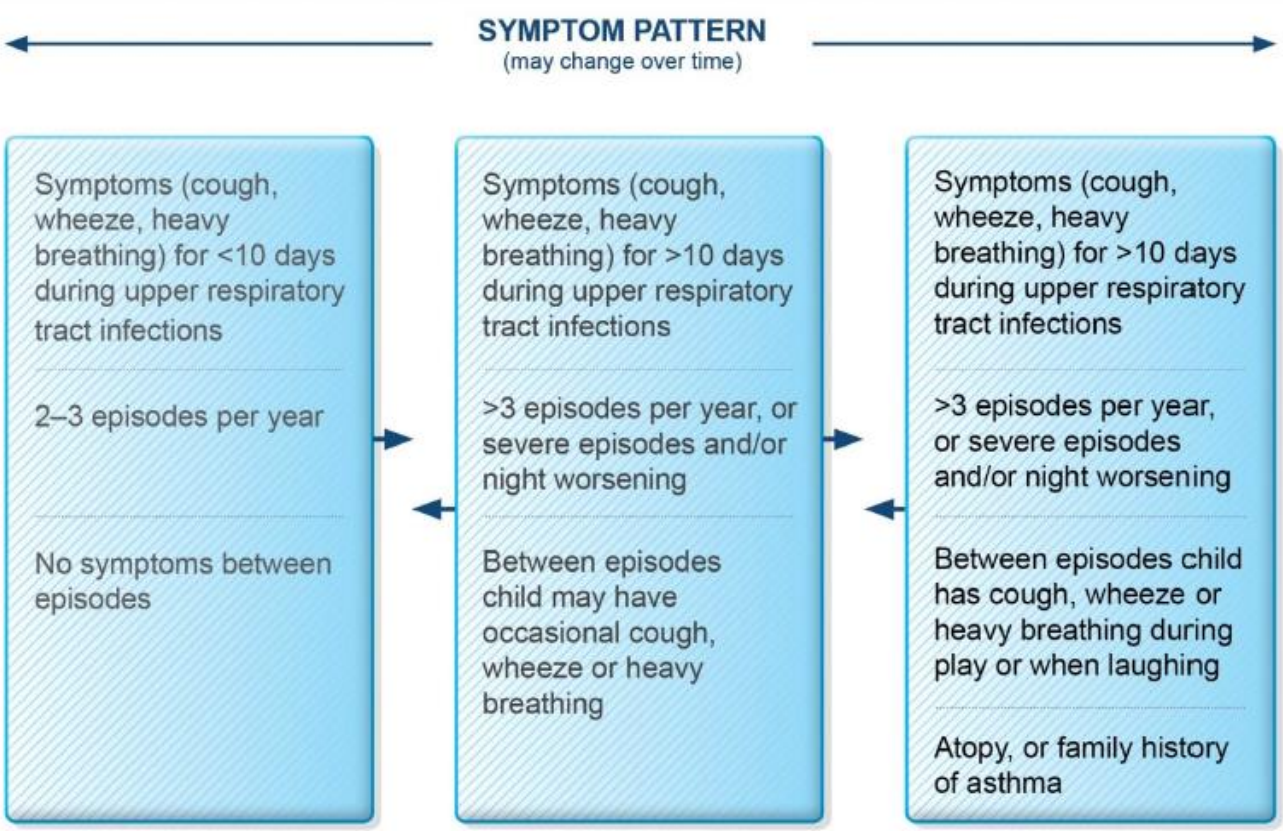

Patient with respiratory symptoms
Are the symptoms typical of asthma?
YES
NO
Detailed history/examination for asthma
History/examination supports asthma diagnosis?
NO
Further history and tests for alternative diagnoses
Alternative diagnosis confirmed?
Clinical urgency, and other diagnoses unlikely
YES
Perform spirometry/PEF with reversibility test
Results support asthma diagnosis?
NO
YES
Repeat on another occasion or arrange other tests
Confirms asthma diagnosis?
NO
Empiric treatment with ICS and prn SABA
Review response
Diagnostic testing within 1-3 months
YES
NO
YES
Consider trial of treatment for most likely diagnosis, or refer for further investigations
Treat for ASTHMA
Treat for alternative diagnosis

Diagnosis of asthma – physical examination

- Physical examination in people with asthma
  - Often normal
  - The most frequent finding is wheezing on auscultation, especially on forced expiration
- Wheezing is also found in other conditions, for example:
  - Respiratory infections
  - COPD
  - Upper airway dysfunction
  - Endobronchial obstruction
  - Inhaled foreign body
- Wheezing may be absent during severe asthma exacerbations ('silent chest')

Probability of asthma diagnosis or response to asthma treatment in children ≤5 years

Symptom patterns in children ≤5 years



Features suggesting asthma in children ≤5 years

Feature	Characteristics suggesting asthma
Cough	Recurrent or persistent non-productive cough that may be worse at night or accompanied by some wheezing and breathing difficulties. Cough occurring with exercise, laughing, crying or exposure to tobacco smoke in the absence of an apparent respiratory infection
Wheezing	Recurrent wheezing, including during sleep or with triggers such as activity, laughing, crying or exposure to tobacco smoke or air pollution
Difficult or heavy breathing or shortness of breath	Occurring with exercise, laughing, or crying
Reduced activity	Not running, playing or laughing at the same intensity as other children; tires earlier during walks (wants to be carried)
Past or family history	Other allergic disease (atopic dermatitis or allergic rhinitis) Asthma in first-degree relatives
Therapeutic trial with low dose ICS and as-needed SABA	Clinical improvement during 2–3 months of controller treatment and worsening when treatment is stopped

Assessment of asthma

1. Asthma control - two domains
   - Assess symptom control over the last 4 weeks
   - Assess risk factors for poor outcomes, including low lung function
2. Treatment issues
   - Check inhaler technique and adherence
   - Ask about side-effects
   - Does the patient have a written asthma action plan?
   - What are the patient's attitudes and goals for their asthma?
3. Comorbidities
   - Think of rhinosinusitis, GERD, obesity, obstructive sleep apnea, depression, anxiety
   - These may contribute to symptoms and poor quality of life

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

Components of Severity		Classification of Asthma Severity (5–11 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC >85%	• FEV_1 = >80% predicted • FEV_1/FVC >80%	• FEV_1 = 60–80% predicted • FEV_1/FVC = 75–80%	• FEV_1 <60% predicted • FEV_1/FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Therapy (See figure 4–1b for treatment steps.)		Step 1	Step 2	Step 3, medium-dose ICS option	Step 3, medium-dose ICS option, or step 4
				and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.			

A reminder – the key change in GINA 2019

EDITORIAL
GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel[1], J. Mark FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

@ERSpublications
GINA no longer recommends treating adults/adolescents with asthma with short-acting bronchodilators alone. Instead, they should receive symptom-driven (in mild asthma) or a daily corticosteroid-containing inhaler, to reduce risk of severe exacerbations. http://bit.ly/310LLzE

Cite this article as: Reddel HK, FitzGerald JM, Bateman ED, *et al.* GINA 2019: a fundamental change in asthma management. *Eur Respir J* 2019; 53: 1901046 [https://doi.org/10.1183/13993003.01046-2019].

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Background to changes in 2019 - the risks of ‘mild’ asthma

- Patients with apparently mild asthma are at risk of serious adverse events
  - 30–37% of adults with acute asthma
  - 16% of patients with near-fatal asthma
  - 15–20% of adults dying of asthma

  } had symptoms less than weekly in previous 3 months
- Exacerbation triggers are variable (viruses, pollens, pollution, poor adherence)
- Inhaled SABA has been first-line treatment for asthma for 50 years
  - This dates from an era when asthma was thought to be a disease of bronchoconstriction
  - Patient satisfaction with, and reliance on, SABA treatment is reinforced by its rapid relief of symptoms, its prominence in ED and hospital management of exacerbations, and low cost
  - Patients commonly believe that *“My reliever gives me control over my asthma”*, so they often don’t see the need for additional treatment

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Background to changes in 2019 - the risks of SABA-only treatment

- Regular or frequent use of SABA is associated with adverse effects
  - β-receptor downregulation, decreased bronchoprotection, rebound hyperresponsiveness, decreased bronchodilator response
  - Increased allergic response, and increased eosinophilic airway inflammation
- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of ≥3 canisters per year (average 1.7 puffs/day) is associated with higher risk of emergency department presentations
  - Dispensing of ≥12 canisters per year is associated with higher risk of death

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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)*

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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

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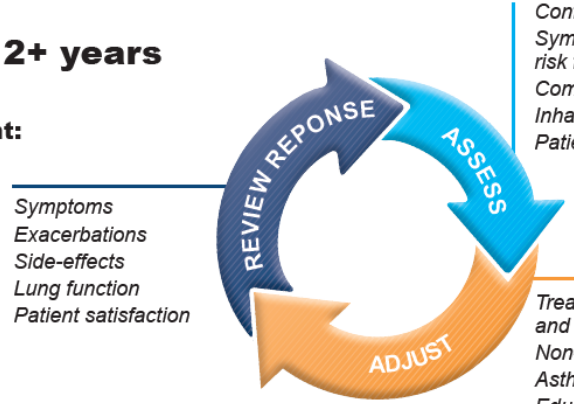
Box 3-5A

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*

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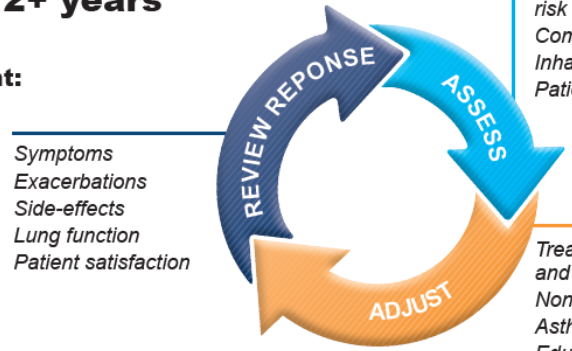
Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response



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Treatment of modifiable ris and comorbidities
Non-pharmacological stra
Asthma medications (adju
Education & skills training

ICS-formoterol is the preferred reliever for patients prescribed maintenance and reliever therapy. For other ICS-LABAs, the reliever is SABA

Asthma medication options:
Adjust treatment up and down for individual patient needs

	STEP 1	STEP 2	STEP 3		
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		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*

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Additional supporting evidence

- Two additional RCTs of as-needed low dose budesonide-formoterol in mild asthma
  - Novel START *(Beasley et al, NEJM 2019, n=668)* and PRACTICAL *(Hardy et al, Lancet 2019, independent study, n=885)*
  - Significant reduction in severe exacerbations vs SABA alone, and vs maintenance ICS, with small or no difference in symptom control, and lower average ICS dose
  - Patients in RCTs of this regimen in mild asthma now total n=9,565
- Both of these studies included inflammatory markers
  - FeNO was significantly reduced by as-needed ICS-formoterol (with average 3-5 doses per week)
  - Reduction in risk of severe exacerbations with as-needed ICS-formoterol was independent of baseline characteristics, including blood eosinophils and exhaled nitric oxide
- An additional RCT of taking ICS whenever SABA is taken (separate inhalers)
  - ASIST, in African-American children 6-17 years with mild asthma, compared with physician-adjusted treatment *(Sumino et al, JACI in Pract 2019, n=206)*

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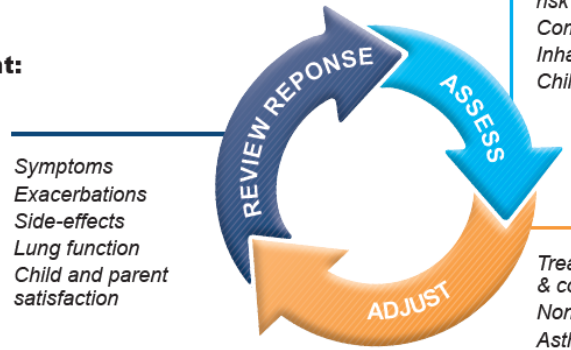
Box 3-5B

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*

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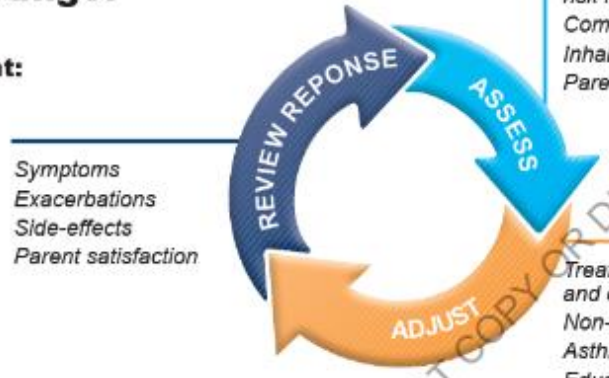
Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



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

Symptoms
Exacerbations
Side-effects
Parent satisfaction

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

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)	Double 'low dose' ICS	Continue controller & refer for specialist assessment
Other controller options		*Daily leukotriene receptor antagonist (LTRA), or intermittent short courses of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	*As-needed short-acting β_2-agonist*			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral. Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Asthma diagnosis, and asthma not well-controlled on low dose ICS Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	Asthma not well-controlled on double ICS

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Initial asthma treatment – where to start?

- Should all patients start at Step 1?
- Table about initial treatment since 2014, but not widely known
  - → New figures created (two versions)

Box 3-4, GINA 2019

Box 3-4. Initial asthma treatment - recommended options for adults and adolescents

Presenting symptoms	Preferred INITIAL treatment
All patients	**SABA-only treatment (without ICS) is not recommended**
Infrequent asthma symptoms, e.g. less than twice a month	• As-needed low dose ICS-formoterol (Evidence B) Other options include taking ICS whenever SABA is taken, in combination or separate inhalers (Evidence B)
Asthma symptoms or need for reliever twice a month or more	• Low dose ICS** with as-needed SABA (Evidence A), or • As-needed low dose ICS-formoterol (Evidence A) Other options include LTRA (less effective than ICS, Evidence A), or taking ICS whenever SABA is taken either in combination or separate inhalers (Evidence B). Consider likely adherence with controller if reliever is SABA.
Troublesome asthma symptoms most days; or waking due to asthma once a week or more, especially if any risk factors exist (Box 2-2B)	• Low dose ICS-LABA† as maintenance and reliever therapy with ICS-formoterol# (Evidence A) or as conventional maintenance treatment with as-needed SABA (Evidence A), OR • Medium dose ICS† with as-needed SABA (Evidence A)
Initial asthma presentation is with severely uncontrolled asthma, or with an acute exacerbation	• Short course of oral corticosteroids AND start regular controller treatment with high-dose ICS (Evidence A), or medium-dose ICS-LABA# (Evidence D)
Before starting initial controller treatment	
• Record evidence for the diagnosis of asthma, if possible • Record the patient's level of symptom control and risk factors, including lung function (Box 2-2, p17) • Consider factors influencing choice between available treatment options (Box 3-3, p27) • Ensure that the patient can use the inhaler correctly • Schedule an appointment for a follow-up visit	
After starting initial controller treatment	
• Review patient's response (Box 2-2, p.31) after 2–3 months, or earlier depending on clinical urgency • See Box 3-5 for recommendations for ongoing treatment and other key management issues • Step down treatment once good control has been maintained for 3 months (Box 3-7, p.56).	

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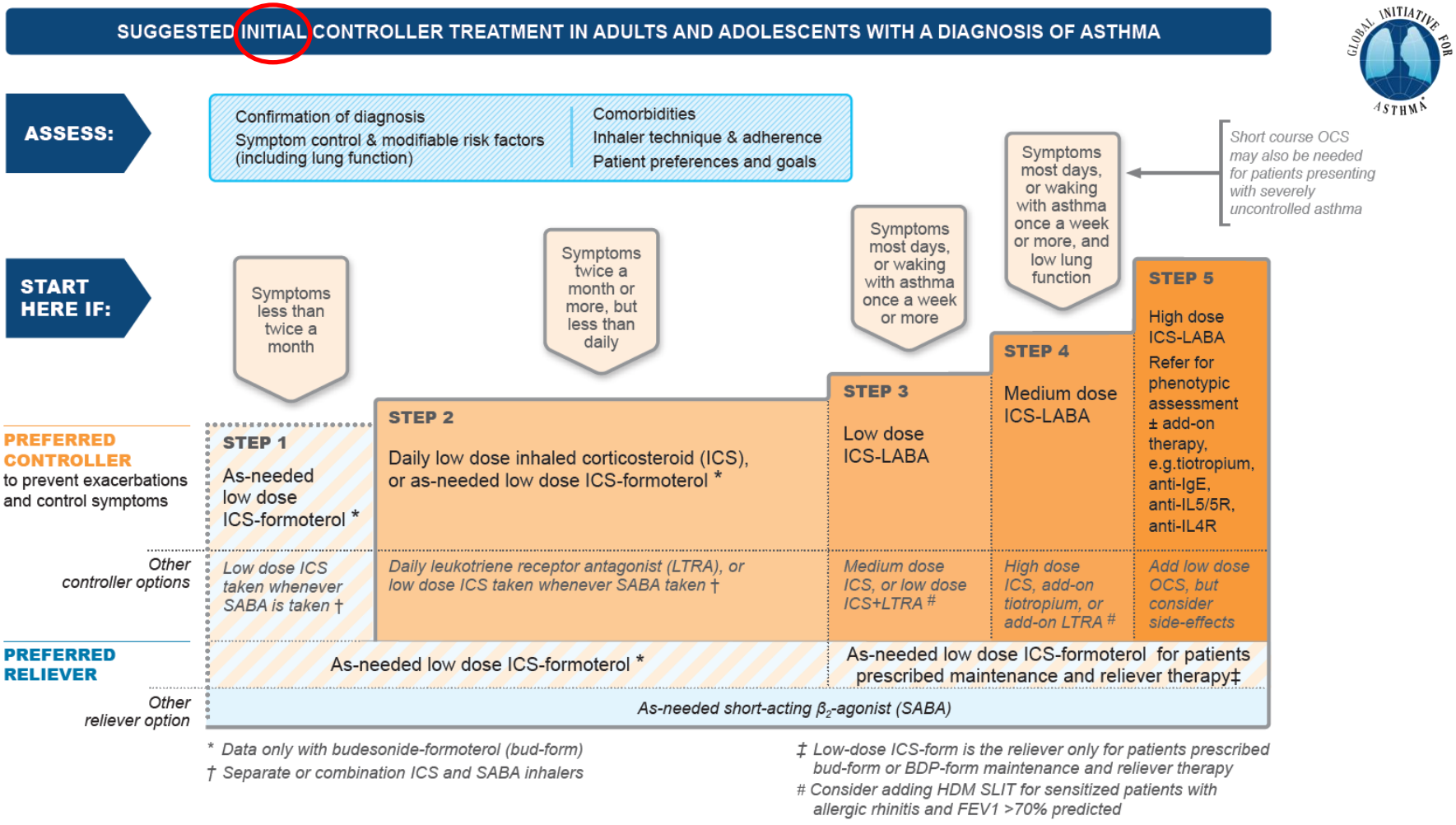
SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA



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\# *Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted*

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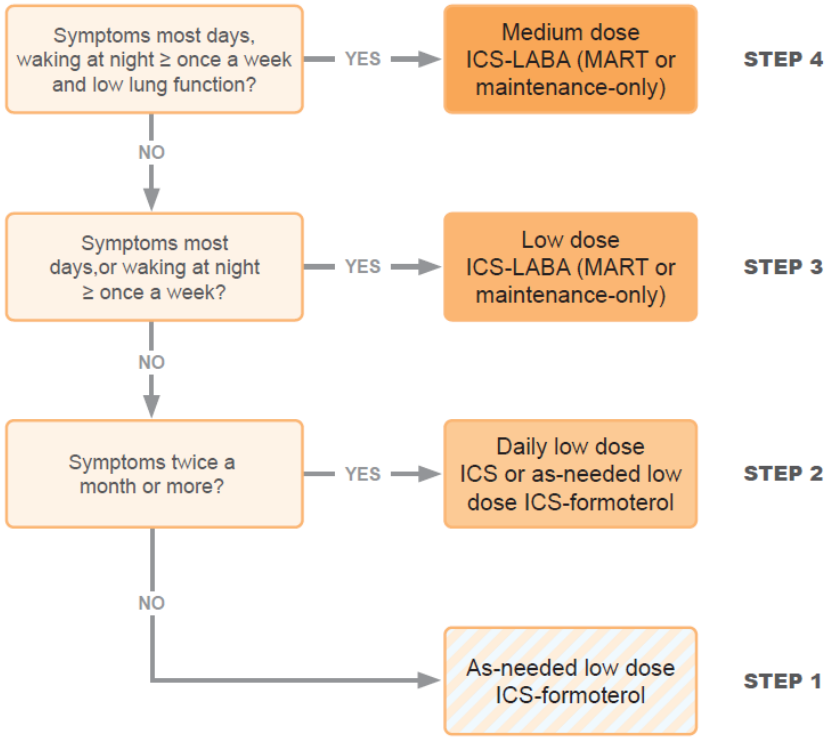
SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA

FIRST ASSESS:

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



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

ASSESS:

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

START HERE IF:

- Symptoms less than twice a month
- Symptoms twice a month or more, but less than daily
- Symptoms most days, or waking with asthma once a week or more
- Symptoms most days, or waking with asthma once a week or more, and low lung function

Short course OCS may also be needed for patients presenting with severely uncontrolled asthma

	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*

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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

IF: / **START WITH:**

Symptoms most days, waking at night ≥ once a week and low lung function?
- YES → Medium dose ICS-LABA or refer for expert advice — **STEP 4**
- NO ↓

Symptoms most days,or waking at night ≥ once a week?
- YES → Low dose ICS-LABA or medium dose ICS — **STEP 3**
- NO ↓

Symptoms twice a month or more?
- YES → Daily low dose ICS — **STEP 2**
- NO ↓

As-needed SABA — **STEP 1**

Short course OCS may also be needed for patients presenting with severely uncontrolled asthma

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As-needed ICS-formoterol – maximum daily dose?

- As-needed low dose budesonide-formoterol
  - Prescribed in maintenance and reliever therapy (Steps 3–5), or as-needed only (Steps 1–2), or within an asthma action plan
  - From product information, the maximum recommended total in one day is 72 mcg formoterol (12 inhalations of budesonide-formoterol Turbuhaler 200/6 mcg)

- As-needed low dose beclometasone-formoterol
  - Prescribed in maintenance and reliever therapy (Steps 3–5), or within an asthma action plan
  - From product information, the maximum recommended total in one day is 48 mcg formoterol (6 inhalations of beclometasone-formoterol pMDI100/6 mcg)

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Assessment of symptom control

- Frequency of SABA use is included in symptom control assessment
  - Higher SABA use is associated with worse outcomes, even in patients taking ICS

Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6–11 years

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• Reliever (SABA) for symptoms more than twice/week?*	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

- Our current view is that frequency of ICS-formoterol use should not be included in symptom control assessment, particularly in patients not taking maintenance ICS
  - The as-needed ICS-formoterol is providing the patient's controller therapy
  - Further data awaited: this issue will be reviewed again next year

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Low, medium and high doses of different ICS

- NOT a table of equivalence
  - Suggested total daily doses for ‘low’, ‘medium’ and ‘high’ dose treatment options
  - Based on available studies (very few) and product information
  - Does NOT imply potency equivalence
- Doses may be country-specific depending on local availability, regulatory labelling and clinical guidelines
- Clinical relevance
  - Low dose ICS provides most of the clinical benefit of ICS for most patients with asthma
  - However, ICS responsiveness varies between patients, so some patients may need medium dose ICS if their asthma is uncontrolled despite good adherence and correct technique
  - High dose ICS (in combination with LABA or separately) is needed by very few patients
    - Its long-term use is associated with an increased risk of local and systemic side-effects, which must be balanced against the potential benefits

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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

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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

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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)

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Asthma management in children

- School-based programs that included asthma self-management are associated with improved asthma outcomes *(Kneale et al, Thorax 2019)*
  - Fewer emergency department visits
  - Fewer hospitalizations
  - Fewer days of reduced activity
- Severe eosinophilic asthma in children aged 6-11 years
  - Mepolizumab approved by European Medicines Agency for this age-group (already approved for 12 years and older)
  - Efficacy data are limited to one small uncontrolled open-label study *(Gupta et al, JACI 2019)*
- Children aged 5 years and younger
  - Assessment of severe exacerbations updated: respiratory rate >40/min added; pulse rate criteria modified; sub-glottic/sub-sternal retractions removed as too subjective

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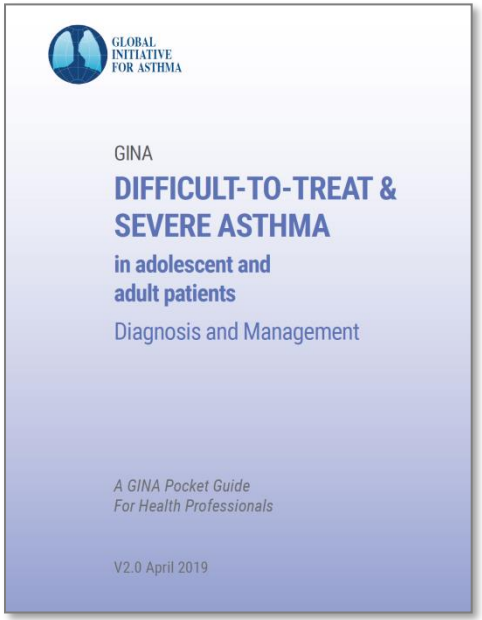
Difficult-to-treat and severe asthma

- Pocket guide v2.0 published April 2019
  - A practical guide for primary and specialist care
  - Includes a decision tree about assessment and management of adults and adolescents with uncontrolled asthma or exacerbations despite Step 4-5 treatment
  - Includes strategies for clinical settings in which biologic therapy is not available or affordable
- Content also included in full GINA 2020 report
- Aim is to produce a similar pocket guide for children in 2020



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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**

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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Acute Asthma and Action Plan

Definition and terminology

- A flare-up or exacerbation is an acute or sub-acute worsening of symptoms and lung function compared with the patient's usual status
- Terminology
  - 'Flare-up' is the preferred term for discussion with patients
  - 'Exacerbation' is a difficult term for patients
  - 'Attack' has highly variable meanings for patients and clinicians
  - 'Episode' does not convey clinical urgency
- Consider management of worsening asthma as a continuum
  - Self-management with a written asthma action plan
  - Management in primary care
  - Management in the emergency department and hospital
  - Follow-up after any exacerbation

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Rationale for change in recommendation about controller therapy in asthma action plans

For the last 10 years, most guidelines recommended treating worsening asthma with SABA alone until OCS were needed, but ...

- Most exacerbations are characterised by increased inflammation
- Most evidence for self-management involved doubling ICS dose
  - Outcomes were consistently better if the action plan prescribed both increased ICS, and OCS
- Lack of generalisability of placebo-controlled RCTs of doubling ICS
  - Participants were required to be highly adherent
  - Study inhalers were not started, on average, until symptoms and airflow limitation had been worsening for 4-5 days.
- Severe exacerbations are reduced by short-term treatment with
  - Quadrupled dose of ICS
  - Quadrupled dose of budesonide/formoterol
  - Early small increase in ICS/formoterol (maintenance & reliever regimen)
- Adherence by community patients is poor
  - Patients commonly take only 25-35% of prescribed controller dose
  - Patients often delay seeking care for fear of being given OCS

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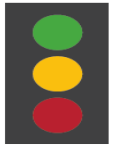
Massachusetts Asthma Action Plan

Name:		Date:
Birth Date:	Doctor/Nurse Name:	Doctor/Nurse Phone #:
Patient Goal:	Parent/Guardian Name & Phone #:	
Important! Avoid things that make your asthma worse:		

Personal Best Peak Flow: _____

The colors of a traffic light will help you use your asthma medicine.



GREEN means Go Zone!
Use controller medicine.

YELLOW means Caution Zone!
Add quick-relief medicine.

RED means Danger Zone!
Get help from a doctor.

GO — You're doing well!

You have *all* of these:

- Breathing is good
- No cough or wheeze
- Sleep through the night
- Can go to school and play

Use these daily controller medicines

Peak flow from ___ to ___	MEDICINE/ROUTE	HOW MUCH	HOW OFTEN/WHEN

CAUTION — Slow Down!

You have *any* of these:

- First signs of a cold
- Cough
- Mild wheeze
- Tight chest
- Coughing, wheezing or trouble breathing at night

Continue with green zone medicine and add:

Peak flow from ___ to ___	MEDICINE/ROUTE	HOW MUCH	HOW OFTEN/WHEN

CALL YOUR DOCTOR/NURSE: _____

DANGER — Get Help!

Your asthma is getting worse fast:

- Medicine is not helping
- Breathing is hard and fast
- Nose opens wide
- Ribs show
- Can't talk well

Take these medicines and call your doctor now.

Peak flow from ___ to ___	MEDICINE/ROUTE	HOW MUCH	HOW OFTEN/WHEN

GET HELP FROM A DOCTOR NOW! Do not be afraid of causing a fuss. Your doctor will want to see you right away. It's important! If you cannot contact your doctor, go directly to the emergency room and bring this form with you. DO NOT WAIT.

Make an appointment with your doctor/nurse within two days of an ER visit or hospitalization.

برنامه درمانی آسم
Asthma Action plan

نام و نام‌خانوادگی: تاریخ تولد: تاریخ مراجعه:
مقدار ایده‌آل پیک‌فلومتری: تاریخ آخرین تزریق واکسن آنفلوانزا:

این برنامه شامل سه مرحله است که با توجه به علائم و نشانه‌های آسم در هر مرحله شما می‌توانید درمان مناسب را بکار برید.
بدیهی است محتوای این برنامه فقط برای شما طراحی شده است و قابل استفاده برای دیگران نمی‌باشد.

مرحله سبز (کم خطر): داروهای کنترلی خود را طبق دستور زیر استفاده نمایید. (اسپری‌ها حتماً با محفظه استفاده شود)

نداشتن سرفه، خس‌خس سینه و تنگی‌نفس
انجام فعالیت روزانه و ورزش بدون محدودیت و سرفه
خواب راحت، بدون سرفه و تنگی‌نفس
مصرف اسپری سالبوتامول ۲ بار یا کمتر در هفته
مقدار پیک فلومتری بیشتر از .....

نام دارو	مقدار مصرف	زمان مصرف

در صورت بروز سرفه هنگام ورزش از اسپری سالبوتامول به مقدار ..... پاف نیم ساعت قبل از ورزش استفاده شود.

مرحله زرد (احتیاط): داروهای کنترلی را ادامه دهید و از داروهای برطرف‌کننده سریع علائم استفاده نمایید.

بروز سرفه، خس‌خس سینه و تنگی‌نفس
شروع علائم سرماخوردگی
محدودیت فعالیت روزانه و تشدید سرفه و تنگی نفس هنگام ورزش و بازی
بیدارشدن از خواب به علت سرفه و تنگی‌نفس
مصرف اسپری سالبوتامول ۳ بار یا بیشتر در هفته
مقدار پیک فلومتری بین ..... و .....

۱. اسپری سالبوتامول ..... پاف هر ۲۰ دقیقه ۳ بار طی یک ساعت
– در صورت برطرف‌شدن علائم بعد از یک ساعت درمان مرحله سبز را ادامه دهید.
– در صورتی که بعد از یک ساعت علائم برطرف‌نشد طبق دستور زیر عمل کنید:
۲. قرص پردنیزولون ..... میلی‌گرمی طبق دستور زیر:

قرص پردنیزلون	روز ۱	روز ۲	روز ۳	روز ۴	روز ۵	روز ۶	روز ۷
صبح							
شب							

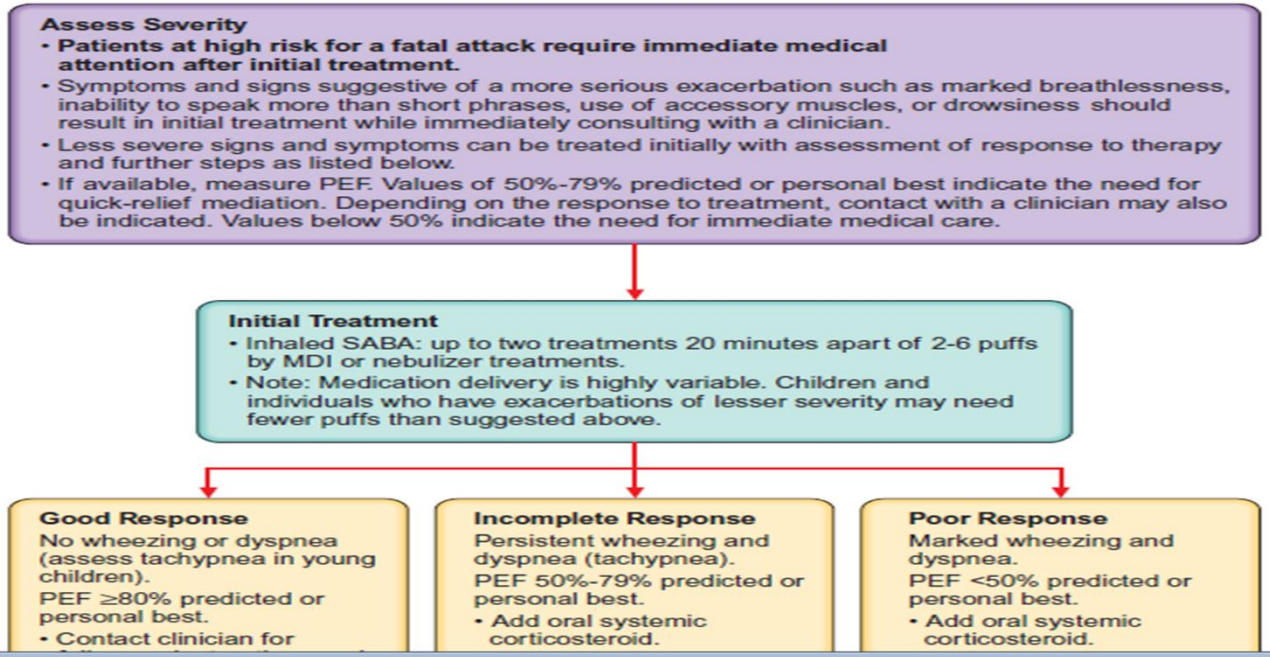
۳. اسپری سالبوتامول ..... پاف هر ..... ساعت به مدت ..... روز
– سایر داروها:
۴. مراجعه به اورژانس: در صورتی که علائم در طی ..... ساعت برطرف‌نشد به اورژانس مراجعه شود.

مرحله قرمز(خطرناک): داروهای کنترلی و داروهای برطرف‌کننده سریع علائم را استفاده نمایید و فوراً به اورژانس مراجعه نمایید.

سرفه‌های مکرر، تنگی‌نفس و خس‌خس شدید سینه
اشکال در نفس کشیدن، تنفس‌های کوتاه و سریع
کبودشدن لب‌ها و ناخن‌ها
عدم توانایی صحبت‌کردن و راه‌رفتن
عدم پاسخ به درمان
مقدار پیک فلومتری کمتر از .....

– تماس سریع با اورژانس و انتقال فوری بیمار به مرکز درمانی
– تا زمان رسیدن به اورژانس از داروی زیر استفاده نمایید:
– اسپری سالبوتامول ..... پاف هر ۱۰ دقیقه

Home Management of asthma exacerbation



Home Management of asthma exacerbation

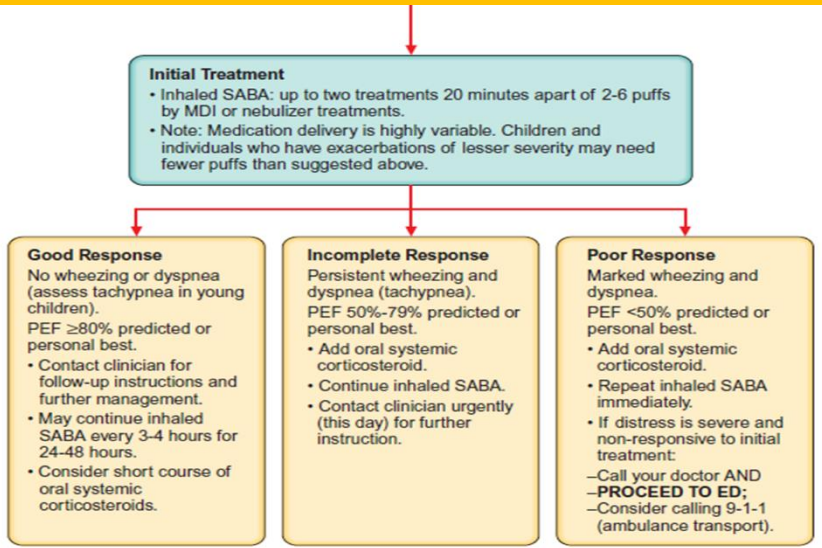


Figure 56-1 Management of asthma exacerbations: Home treatment. *ED*, Emergency department; *MDI*, metered-dose inhaler; *PEF*, peak expiratory flow; *SABA*, short-acting β_2-agonist (quick-relief inhaler). *(From National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Full report 2007. Washington D.C.: US Government Printing Office; 2007.)*

Managing exacerbations in primary care

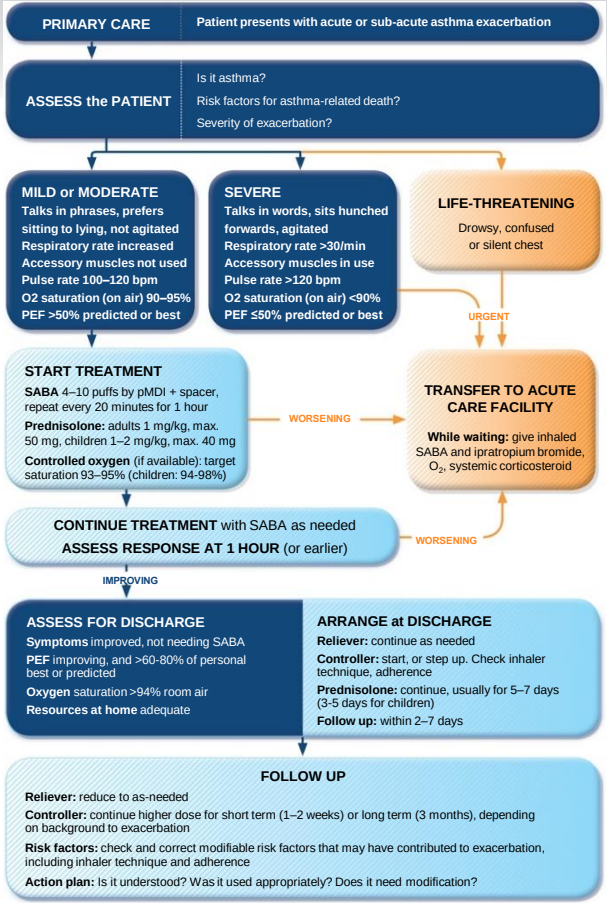


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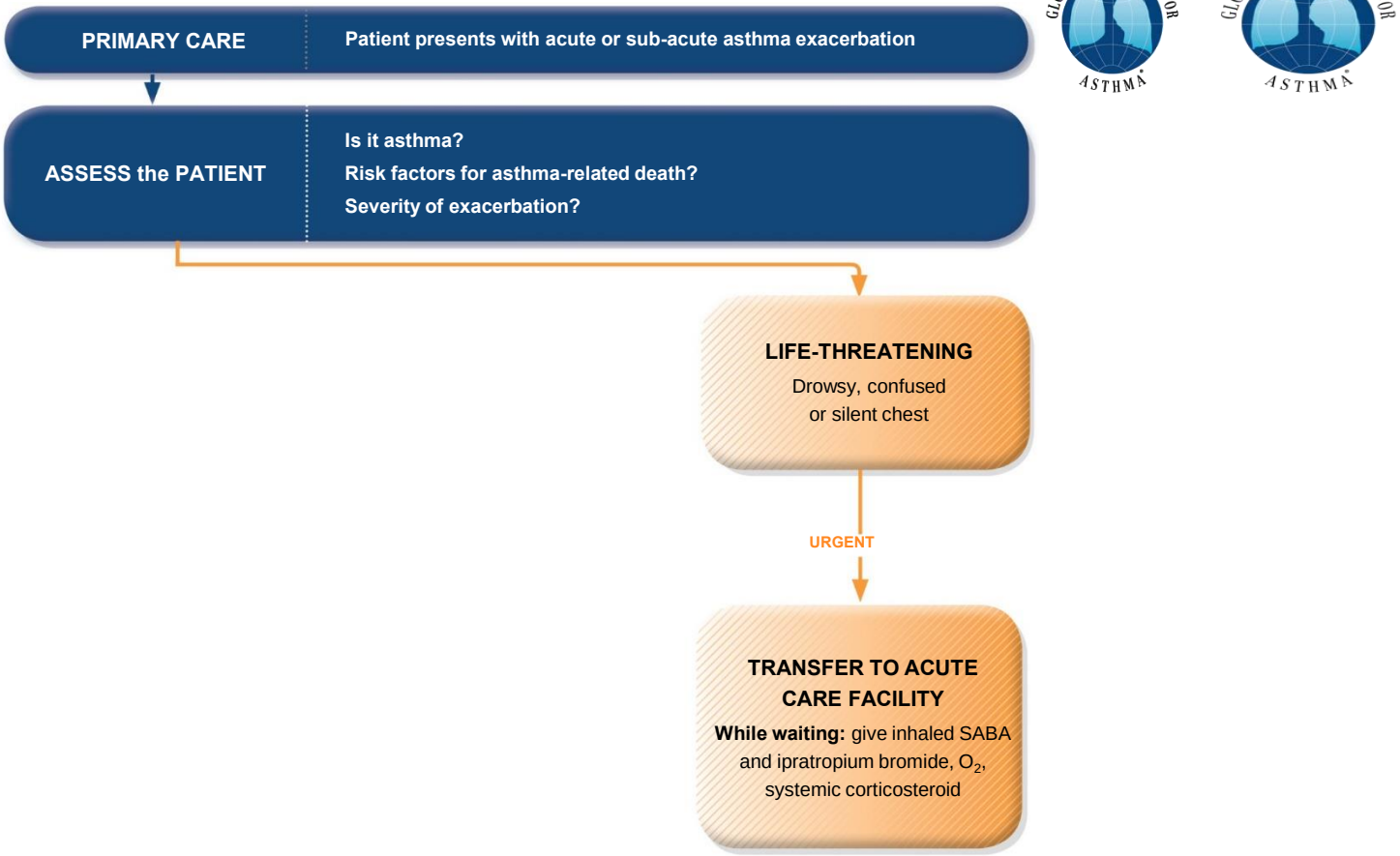
Table 138-4 FORMAL EVALUATION OF ASTHMA EXACERBATION SEVERITY IN THE URGENT OR EMERGENCY CARE SETTING*

	MILD	MODERATE	SEVERE	SUBSET: RESPIRATORY ARREST IMMINENT
SYMPTOMS				
Breathlessness	While walking	While at rest (infant—softer, shorter cry, difficulty feeding)	While at rest (infant—stops feeding)	
	Can lie down	Prefers sitting	Sits upright	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
SIGNS				
Respiratory rate†	Increased	Increased	Often >30 breaths/min	
Use of accessory muscles; suprasternal retractions	Usually not	Commonly	Usually	Paradoxical thoracoabdominal movement
Wheeze	Moderate; often only end-expiratory	Loud; throughout exhalation	Usually loud; throughout inhalation and exhalation	Absence of wheeze
Pulse rate (beats/min)‡	<100	100-120	>120	Bradycardia
Pulsus paradoxus	Absent <10 mm Hg	May be present 10-25 mm Hg	Often present >25 mm Hg (adult) 20–40 mm Hg (child)	Absence suggests respiratory muscle fatigue
FUNCTIONAL ASSESSMENT				
Peak expiratory flow (value predicted or personal best)	≥70%	Approx. 40-69% or response lasts <2 hr	<40%	<25%§
Pao_2 (breathing air) *and/or*	Normal (test not usually necessary)	≥60 mm Hg (test not usually necessary)	<60 mm Hg; possible cyanosis	
Pco_2	<42 mm Hg (test not usually necessary)	<42 mm Hg (test not usually necessary)	≥42 mm Hg; possible respiratory failure	
Sao_2 (breathing air) at sea level	>95% (test not usually necessary)	90-95% (test not usually necessary)	<90%	
	Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents			

*Notes:
- The presence of several parameters, but not necessarily all, indicates the general classification of the exacerbation.
- Many of these parameters have not been systematically studied, especially as they correlate with each other. Thus, they serve only as general guides.
- The emotional impact of asthma symptoms on the patient and family is variable but must be recognized and addressed and can affect approaches to treatment and follow-up.

†Normal breathing rates in awake children by age: <2 mo, <60 breaths/min; 2-12 mo, <50 breaths/min; 1-5 yr, <40 breaths/min; 6-8 yr, <30 breaths/min.
‡Normal pulse rates in children by age: 2-12 mo, <160 beats/min; 1-2 yr, <120 beats/min; 2-8 yr, <110 beats/min.
§Peak expiratory flow testing may not be needed in very severe attacks.
Modified from EPR—3. Expert panel report 3: guidelines for the diagnosis and management of asthma. NIH Publication No. 07-4051, Bethesda, MA, 2007, U.S. Department of Health and Human Services; National Institutes of Health, National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm.



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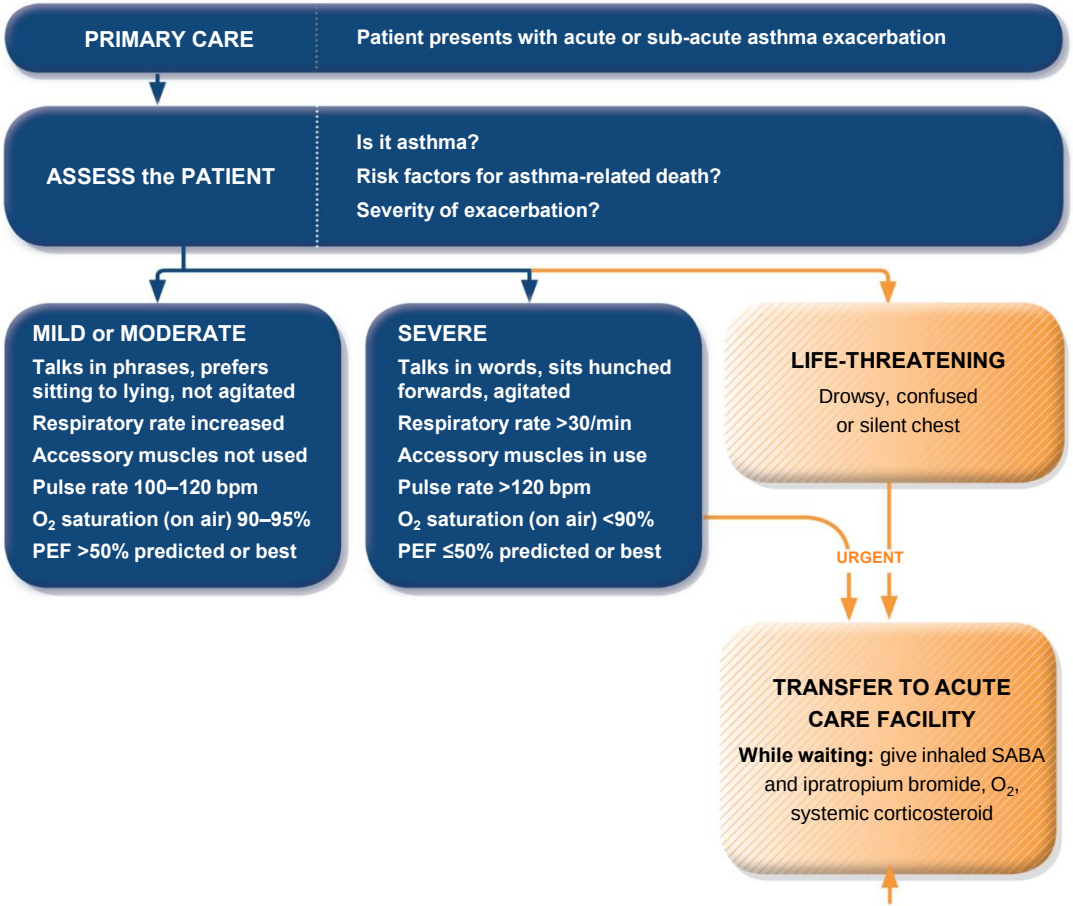

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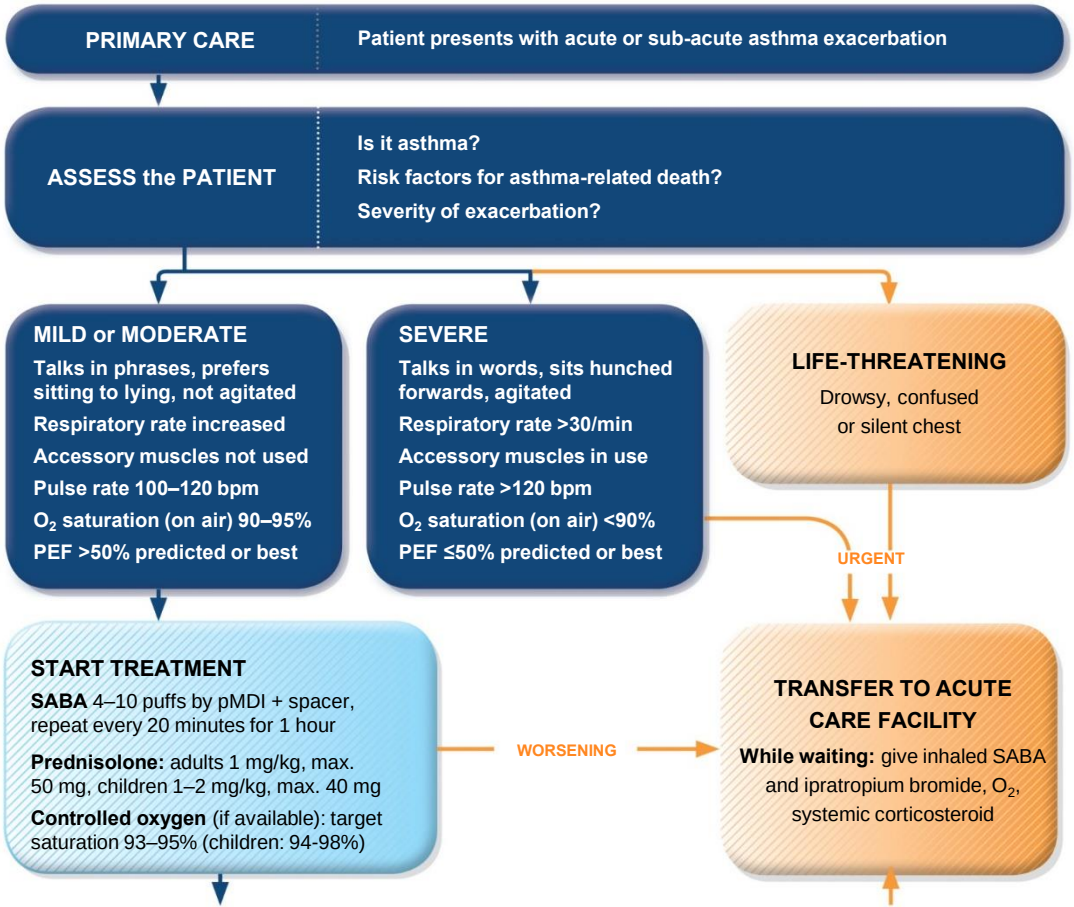

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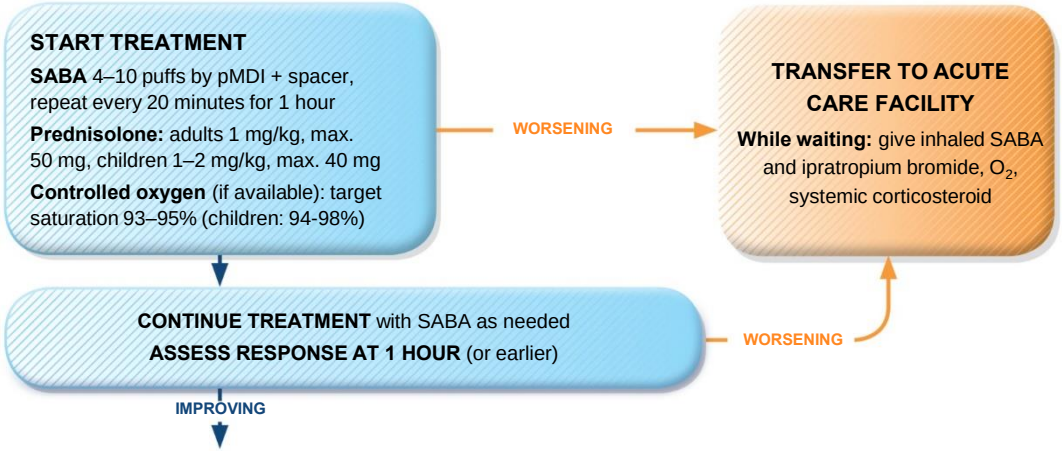

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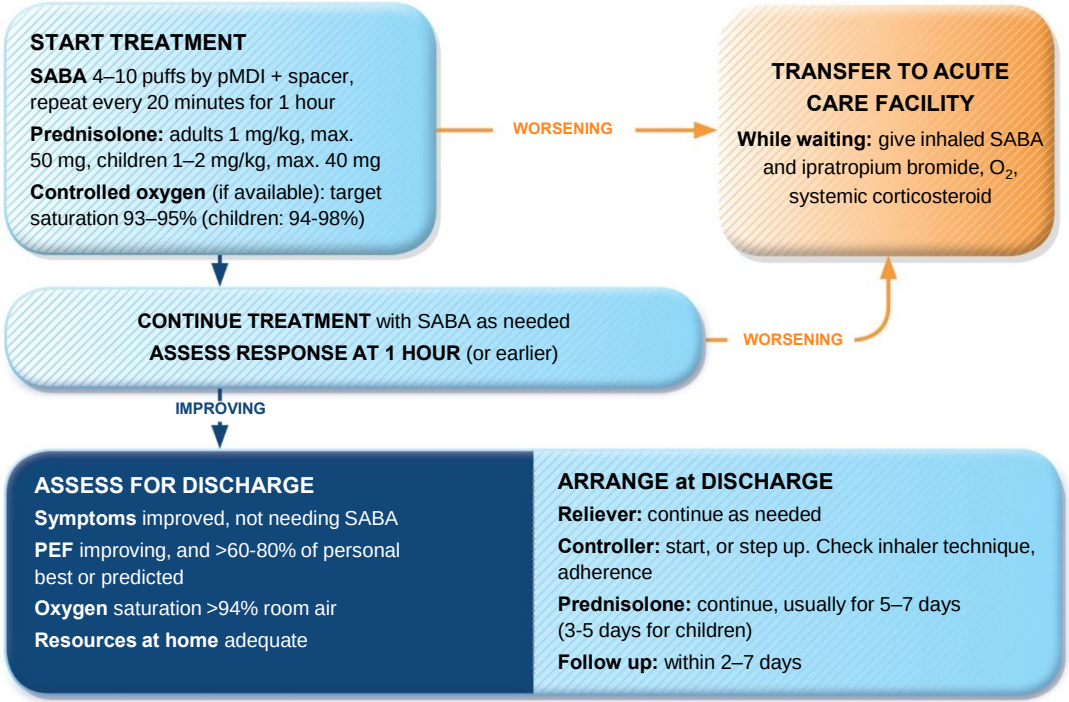

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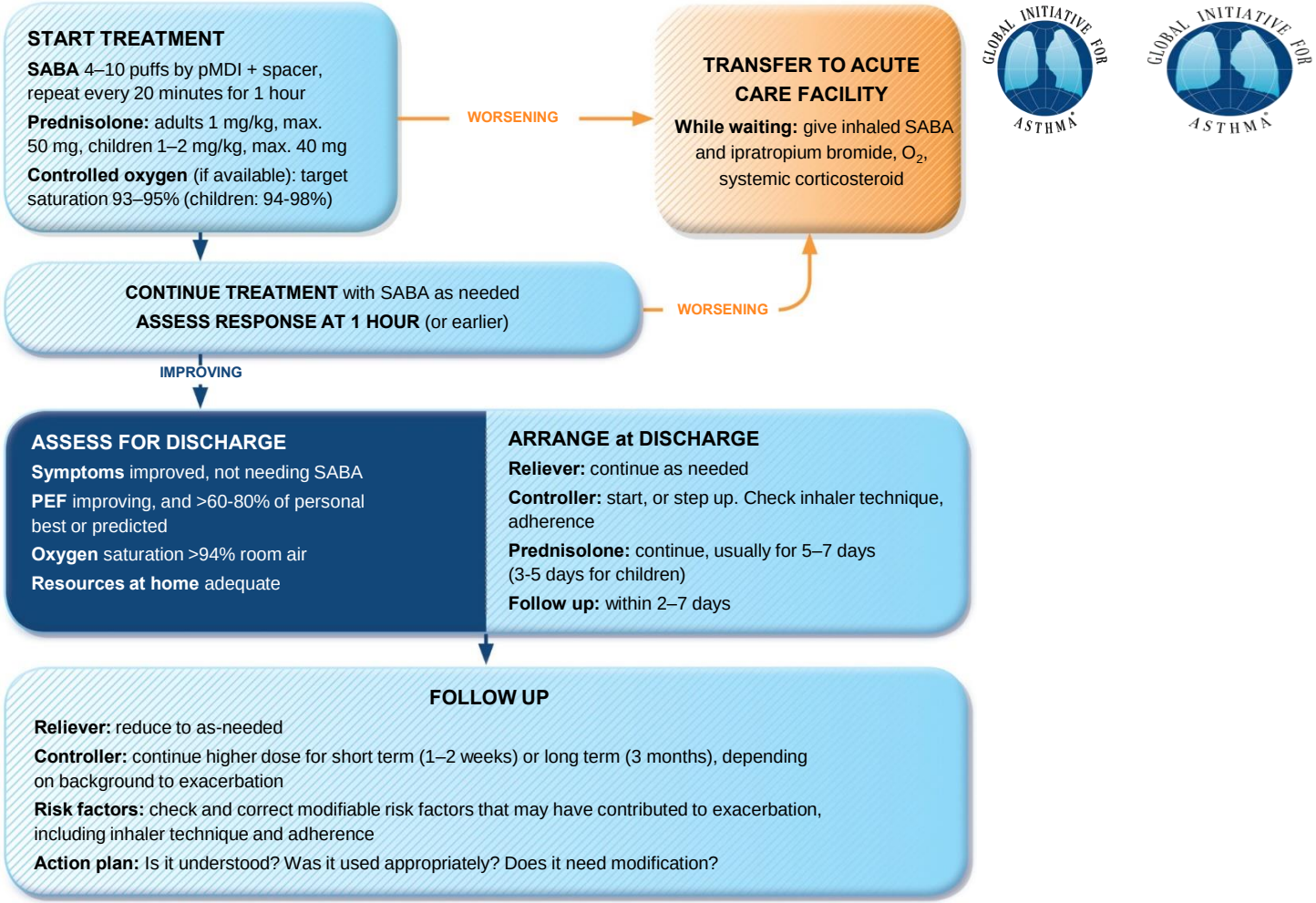

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Dosages of Drugs for Asthma Exacerbations

SYSTEMIC (INJECTED) β_2-AGONSTS			
Epinephrine 1:1000 (1 mg/mL)	0.01 mg/kg up to 0.3-0.5 mg every 20 min for 3 doses SQ	0.3-0.5 mg every 20 min for 3 doses SQ	No proven advantage of systemic therapy over aerosol
Terbutaline (1 mg/mL)	0.01 mg/kg every 20 min for 3 doses SQ, then every 2-6 h as needed	0.25 mg every 20 min for 3 doses SQ	No proven advantage of systemic therapy over aerosol
ANTICHOLINERGICS			
IPRATROPIUM BROMIDE			
Nebulizer solution (0.25 mg/mL)	0.25-0.5 mg every 20 min for 3 doses, then as needed	0.5 mg every 20 min for 3 doses, then as needed	May mix in same nebulizer with albuterol; should not be used as first-line therapy; should be added to SABA therapy for severe exacerbations; addition of ipratropium not shown to provide further benefit after patient is hospitalized
MDI (18 µg/puff)	4-8 puffs every 20 min as needed up to 3 h	8 puffs every 20 min as needed up to 3 h	Should use with VHC and face mask for children <4 yr; studies have examined ipratropium bromide MDI for up to 3 h
IPRATROPIUM WITH ALBUTEROL			
Nebulizer solution (each 3-mL vial contains 0.5 mg ipratropium bromide and 2.5 mg albuterol)	1.5 mL every 20 min for 3 doses, then as needed	3 mL every 20 min for 3 doses, then as needed	May be used for up to 3 h in initial management of severe exacerbations; addition of ipratropium to albuterol not shown to provide further benefit after patient is hospitalized
MDI (each puff contains 18 µg ipratropium bromide and 90 µg of albuterol)	4-8 puffs every 20 min as needed up to 3 h	8 puffs every 20 min as needed up to 3 h	Should use with VHC and face mask for children <4 yr

Dosages of Drugs for Asthma Exacerbations

TABLE 56-1 Dosages of Drugs for Asthma Exacerbations—cont'd

Medications	DOSAGES: Children*	DOSAGES: Adults	Comments
SYSTEMIC CORTICOSTEROIDS†			
Prednisone Methylprednisolone Prednisolone	1 mg/kg in 2 divided doses (maximum, 60 mg/day) until PEF is 70% of predicted or personal best	40-80 mg/day in 1 or 2 divided doses until PEF reaches 70% of predicted or personal best	For outpatient burst, use 40-60 mg in single dose or 2 divided doses for total of 5-10 days in adults (children: 1-2 mg/kg/day maximum, 60 mg/day for 3-10 days)

From National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Full report 2007. Washington D.C.: US Government Printing Office; 2007.

ED, Emergency department; *ICs*, inhaled corticosteroids; *MDI*, metered-dose inhaler; *PEF*, peak expiratory flow; *SABA*, short-acting β_2-agonists; *VHC*, valved holding chamber.

*Children ≤12 years of age.

†Dosages and comments apply to all three corticosteroids. There is no known advantage for higher doses of corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration over oral therapy if gastrointestinal transit time or absorption is not impaired. The total course of systemic corticosteroids for an asthma exacerbation requiring an ED visit or hospitalization may be 3 to 10 days. For corticosteroid courses of less than 1 week, there is no need to taper the dose. For slightly longer courses (e.g., up to 10 days), there probably is no need to taper, especially if patients are concurrently taking ICs. The ICs can be started at any point in the treatment of an asthma exacerbation.

Magnesium Sulfate

- This agent has immediate bronchodilator effects
  and mild anti inflammatory effects.
- magnesium is safe and effective in patients with severe exacerbations.
- guidelines recommend consideration of intravenous $MgSO_4$ in patients who have life-threatening exacerbations
- and in those whose exacerbations remains in the severe category after 1 hour of intensive conventional therapy.

The recommended dose of magnesium sulfate is

2 gr given intravenously over 20 minutes in adults

And 25 to 100 mg/kg in children (total maximum dose of 2 g)

Other changes in GINA 2020

- Acute asthma
  - References to ‘high flow oxygen’ have been corrected to ‘high concentration oxygen’
- Role of trained lay health workers in asthma education has been emphasized
  - Improved outcomes compared with usual care including increased symptom-free days, reduced healthcare utilization, improved adherence, inhaler technique, symptom control and quality of life
- Factors contributing to development of asthma
  - Obesity may be a risk factor for developing asthma *(Deng et al, Pediatr Obes 2019)*, but not vice versa *(Xu et al, Int J Epidemiol 2019)*
  - 13% of global asthma incidence in children may be attributable to traffic-related air pollution *(Achakulwisut et al, Lancet Plan Health 2019)*

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COVID-19 and asthma

- 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
- *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

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راهنمای بالینی پیشگیری، تشخیص و درمان آسم

(در بزرگسالان و کودکان بالای ۵ سال)

GLOBAL INITIATIVE FOR ASTHMA

راهنمای جیبی برای پزشکان

نسخه سال ۲۰۲۰

ویراستاران:

دکتر محمد رضا فضل الهی
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی تهران
دکتر مهران قسمتی زاده
پزشک عمومی، دبیر کمیته آموزش انجمن پزشکان عمومی ایران
دکتر بابک قلعه باغی
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی ایران

مترجمین

دکتر نرگس اسلامی
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی شهید بهشتی
دکتر حسین اسماعیل زاده
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی شیراز
دکتر مهدی ترابی زاده
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی اهواز
دکتر عباس دباغ زاده
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی مازندران
دکتر فرشته سالاری
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی ایران
دکتر مرتضی فلاح پور
فوق تخصص آلرژی و ایمونولوژی بالینی، دانشگاه علوم پزشکی ایران

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Questions?

GINA Global Strategy for Asthma Management and Prevention

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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

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Other resources for COVID-19 *(as at March 30, 2020)*

- Information for health professionals
  - World Health Organization (WHO) recommendations for infection control www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125
  - Centers for Disease Control and Prevention (CDC) www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html,
- Information for patients
  - CDC: https://www.cdc.gov/coronavirus/2019-ncov/index.html.
- Information for health systems
  - www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance
- Follow local health advice about hygiene strategies and use of personal protective equipment as new information becomes available in your country or region

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About the GINA strategy

- The GINA report is not a guideline, but an integrated evidence-based strategy focusing on translation into clinical practice
- Recommendations are framed, not as answers to isolated PICOT questions, but as part of an integrated strategy, in relation to:
  - The GINA goals of preventing asthma deaths and exacerbations, as well as improving symptom control
  - Current understanding of underlying disease processes
  - Human behavior (of health professionals and patients/carers)
  - Implementation in clinical practice
  - Global variation in populations, health systems and medication access

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Patients with features of asthma and COPD

- Also called ‘asthma-COPD overlap’ or ‘asthma+COPD’
  - NOT a single disease, but a descriptive label for patients commonly seen in clinical practice
- Asthma and COPD are heterogeneous and overlapping conditions
  - The definitions of asthma and COPD are not mutually exclusive
  - Each includes several phenotypes that are likely to have different underlying mechanisms
  - There is increasing interest in the potential for precision treatment
- However, the labels ‘asthma’ and ‘COPD’ are still clinically important, as evidence supports safety-based differences in treatment recommendations
  - Asthma: never treat with bronchodilators alone (risk of death, hospitalization, severe exacerbations)
  - COPD: start treatment with LABA and/or LAMA without ICS
  - Patients with diagnoses of both asthma and COPD are more likely to die or be hospitalized if treated with LABA vs ICS-LABA *(Gershon et al, JAMA 2014; Kendzerska et al, Annals ATS 2019)*
  - High dose ICS may be needed for severe asthma, but should not be used in COPD (risk of pneumonia)
- Chapter 5 has been rewritten for clinical utility, focusing on clinical recognition and safe initial treatment

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Patients with features of asthma and COPD

CLINICAL PHENOTYPE - ADULTS WITH CHRONIC RESPIRATORY SYMPTOMS (dyspnea, cough, chest tightness, wheeze)

HIGHLY LIKELY TO BE ASTHMA if several of the following features TREAT AS ASTHMA	FEATURES OF BOTH ASTHMA + COPD TREAT AS ASTHMA	LIKELY TO BE COPD if several of the following features TREAT AS COPD

HISTORY
• Symptoms vary over time and in intensity
  - Triggers may include laughter, exercise, allergens, seasonal
  - Onset before age 40 years
  - Symptoms improve spontaneously or with bronchodilators (minutes) or ICS (days to weeks)
• Current asthma diagnosis, or asthma diagnosis in childhood
LUNG FUNCTION
• Variable expiratory airflow limitation
• Persistent airflow limitation may be present
	HISTORY
	• Symptoms intermittent or episodic
	  - May have started before or after age 40
	• May have a history of smoking and/or other toxic exposures, or history of low birth weight or respiratory illness such as tuberculosis
	• Any of asthma features at left (e.g. common triggers; symptoms improve spontaneously or with bronchodilators or ICS; current asthma diagnosis or asthma diagnosis in childhood)
	LUNG FUNCTION
	• Persistent expiratory airflow limitation
	• With or without bronchodilator reversibility
		HISTORY
		• Dyspnea persistent (most days)
		  - Onset after age 40 years
		  - Limitation of physical activity
		  - May have been preceded by cough/sputum
		  - Bronchodilator provides only limited relief
		• History of smoking and/or other toxic exposure, or history of low birth weight or respiratory illness such as tuberculosis
		• No past or current diagnosis of asthma
		LUNG FUNCTION
		• Persistent expiratory airflow limitation
		• With or without bronchodilator reversibility

INITIAL PHARMACOLOGICAL TREATMENT (as well as treating comorbidities and risk factors. See Box 3-5A)

• **ICS-CONTAINING TREATMENT IS ESSENTIAL to reduce risk of severe exacerbations and death.** See Box 3-5A
  - As-needed low dose ICS-formoterol may be used as reliever. See Box 3-5A
• **DO NOT GIVE LABA and/or LAMA without ICS**
• Avoid maintenance OCS
	• **ICS-CONTAINING TREATMENT IS ESSENTIAL to reduce risk of severe exacerbations and death.** See Box 3-5A
	• Add-on LABA and/or LAMA usually also needed
	• Additional COPD treatments as per GOLD
	• **DO NOT GIVE LABA and/or LAMA without ICS**
	• Avoid maintenance OCS
		• **TREAT AS COPD (see GOLD report)**
		  - Initially LAMA and/or LABA
		  - Add ICS as per GOLD for patients with hospitalizations, ≥2 exacerbations/year requiring OCS, or blood eosinophils ≥300/µl
		• Avoid high dose ICS, avoid maintenance OCS
		• Reliever containing ICS is not recommended

REVIEW PATIENT AFTER 2-3 MONTHS. REFER FOR EXPERT ADVICE IF DIAGNOSTIC UNCERTAINTY OR INADEQUATE RESPONSE

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GINA methodology – additional details

- The GINA report is a global strategy document
  - Regulatory approvals and submissions differ from country to country
  - Many recommendations are ‘off-label’ in various countries, particularly for paediatrics
  - → The term ‘off-label’ is no longer used in the GINA report or slides
- For new therapies
  - Regulatory agencies often receive more safety data than are in peer-reviewed literature
  - → GINA makes recommendations based on the best available evidence, after approval by at least one major regulatory agency (e.g. EMA, FDA)
- For existing medications with evidence for new regimens or populations
  - If satisfied with evidence for safety and effectiveness, GINA may consider making recommendations that are not covered by a regulatory indication in any country at the time
  - Examples: long-term macrolides for moderate-severe asthma (2018); as-needed ICS-formoterol, or taking ICS whenever SABA is taken, for mild asthma (2019)
- When assessing and treating patients
  - Use your own professional judgment
  - Take into account local and national guidelines and payer eligibility criteria, and licensed drug doses

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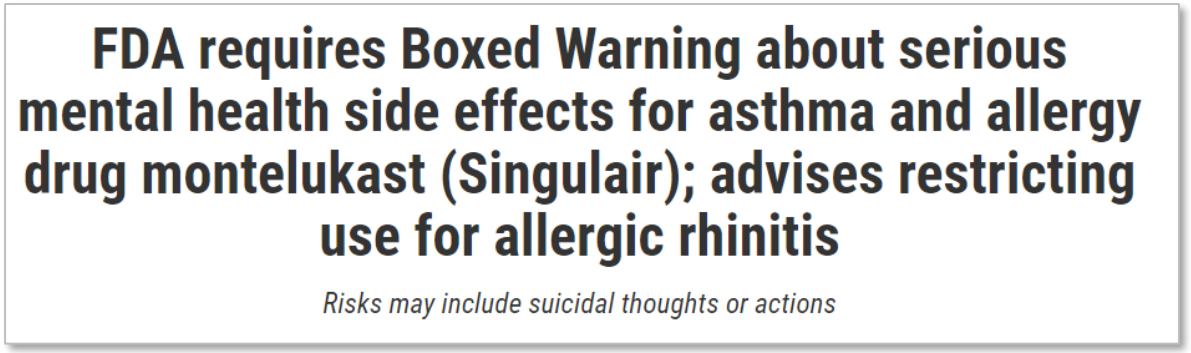
Components of Control		Classification of Asthma Control (0–4 years of age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	>1x/month	>1x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
Risk	**Exacerbations requiring oral systemic corticosteroids**	**0–1/year**	**2–3/year**	**>3/year**
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment **(See figure 4–1a for treatment steps.)**		• Maintain current treatment. • Regular followup every 1–6 months. • Consider step down if well controlled for at least 3 months.	• Step up (1 step) and • Reevaluate in 2–6 weeks. • If no clear benefit in 4–6 weeks, consider alternative diagnoses or adjusting therapy. • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up (1–2 steps), and • Reevaluate in 2 weeks. • If no clear benefit in 4–6 weeks, consider alternative diagnoses or adjusting therapy. • For side effects, consider alternative treatment options.

Components of Control		Classification of Asthma Control (5–11 years of age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week but not more than once on each day	>2 days/week or multiple times on ≤2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	≥2x/month	≥2x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	Lung function • FEV_1 or peak flow • FEV_1/FVC	 >80% predicted/ personal best >80%	 60–80% predicted/ personal best 75–80%	 <60% predicted/ personal best <75%
Risk	**Exacerbations requiring oral systemic corticosteroids**	**0–1/year**	**≥2/year (see note)**	
		Consider severity and interval since last exacerbation		
	Reduction in lung growth	Evaluation requires long-term followup.		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment **(See figure 4–1b for treatment steps.)**		• Maintain current step. • Regular followup every 1–6 months. • Consider step down if well controlled for at least 3 months.	• Step up at least 1 step and • Reevaluate in 2–6 weeks. • For side effects: consider alternative treatment options.	• Consider short course of oral systemic corticosteroids, • Step up 1–2 steps, and • Reevaluate in 2 weeks. • For side effects, consider alternative treatment options.

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

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