Global Initiative for Asthma (GINA)

What's new in GINA 2020?

GINA Global Strategy for Asthma Management and Prevention

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
  - For patients with severe asthma: continue biologic therapy, and do not suddenly stop OCS
- Make sure that all patients have a *written asthma action plan* with instructions

- *Avoid nebulizers* where possible
  - Nebulizers increase the risk of disseminating virus to other patients AND to health care professionals
  - pMDI via a spacer is preferred except for life-threatening exacerbations
    - Add a mouthpiece or tightly fitting mask to the spacer if required

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

- *Avoid spirometry* in patients with confirmed/suspected COVID-19
  - Spirometry can disseminate viral particles and expose staff and patients to risk of infection
  - Postpone spirometry and peak flow measurement within health care facilities unless urgent needs

- At present, based on the risks and benefits, GINA recommends COVID-19 vaccination for people with asthma

- anaphylaxis can be treated if it occurs, and they should not be administered to patients with a history of severe allergic reaction to polyethylene glycol,
or any other vaccine ingredient.

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].

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 *(Dusser, Allergy 2007)*

- 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

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 *(Hancox, Respir Med 2000)*
  - Increased allergic response, and increased eosinophilic airway inflammation *(Aldridge, AJRCCM 2000)*

- 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 *(Stanford, AAAI 2012)*
  - Dispensing of ≥12 canisters per year is associated with higher risk of death *(Suissa, AJRCCM 1994)*

The 12-year history behind changes in GINA 2019

- Since 2007, GINA has been actively seeking interventions for mild asthma
  - to reduce the risk of asthma-related exacerbations and death
  - to provide consistent messaging about the goals of asthma treatment, including prevention of exacerbations, across the spectrum of asthma severity
  - to avoid establishing patient reliance on SABA early in the course of the disease
- GINA emphasized poor adherence as a modifiable risk factor for exacerbations
  - When the reliever is SABA, poor adherence with maintenance controller exposes the patient to risks of SABA-only treatment
- GINA members repeatedly sought funding for RCTs of as-needed ICS-formoterol for risk reduction in mild asthma
  - Eventually culminated in 2014 with the initiation of the SYGMA studies, published in 2018 *(O'Byrne NEJMed 2018; Bateman NEJMed 2018)*

GINA 2019 – landmark changes in asthma management

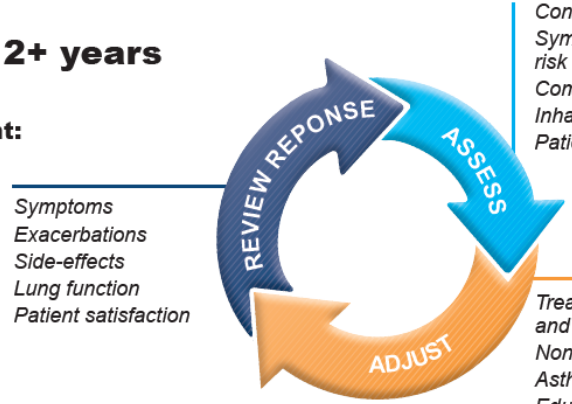
- For safety, GINA no longer recommends SABA-only treatment for Step 1
  - This decision was based on evidence that SABA-only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk

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

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

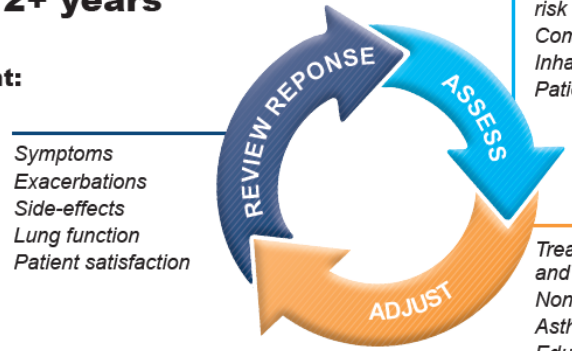
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic 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*

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 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*

Additional supporting evidence

- Two additional RCTs of as-needed low dose budesonide-formoterol in mild asthma
  - 12-month studies, open-labe
  - 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

- 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*(Sumino et al, JACI in Pract 2019, n=206)*

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)

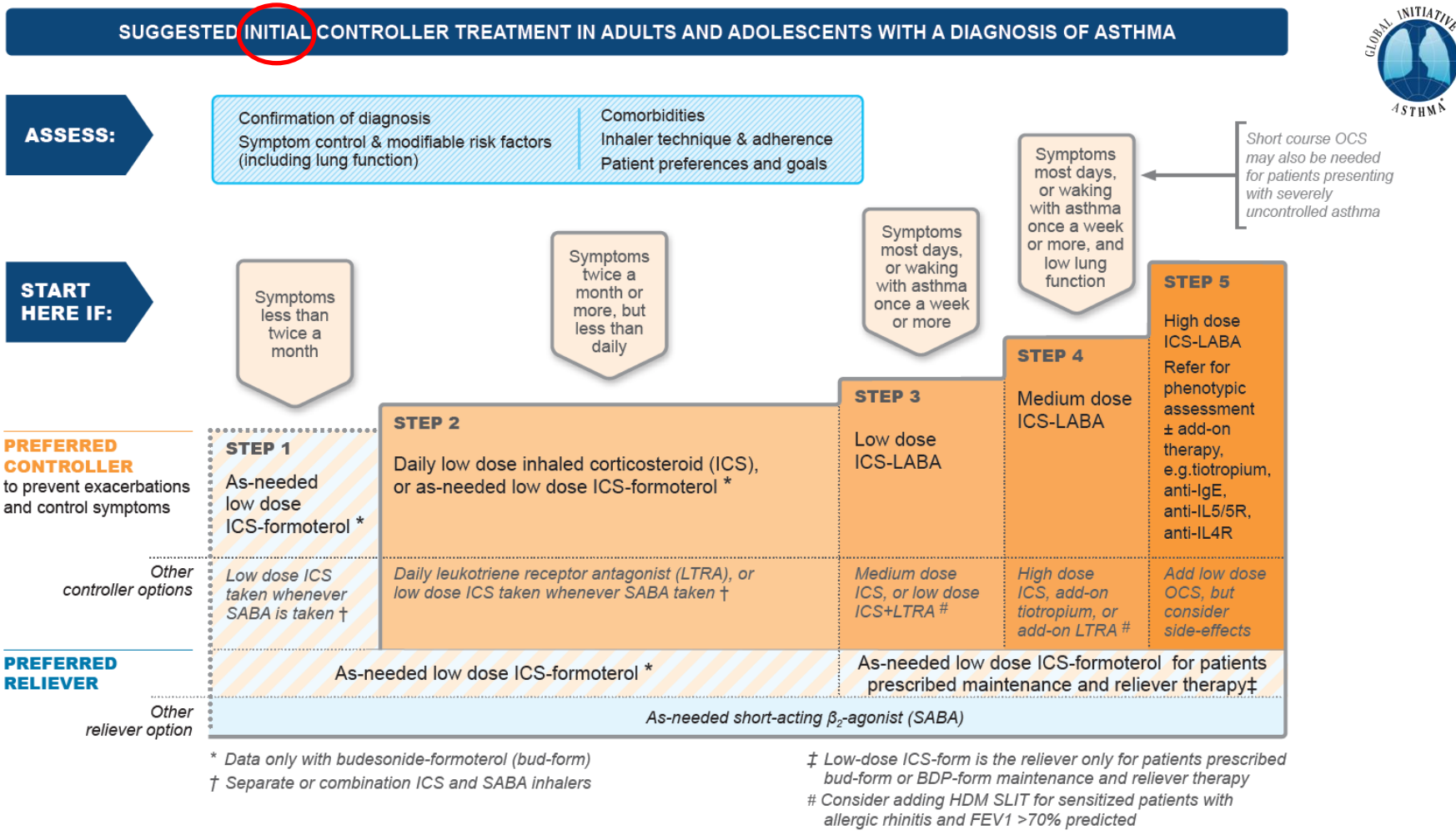
Before starting initial controller treatment

- 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).

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



* *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*

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

IF: / **START WITH:**

- Symptoms most days, waking at night ≥ once a week and low lung function? — YES → Medium dose ICS-LABA (MART or maintenance-only) — **STEP 4**
  - *Short course OCS may also be needed for patients presenting with severely uncontrolled asthma*
- NO → Symptoms most days,or waking at night ≥ once a week? — YES → Low dose ICS-LABA (MART or maintenance-only) — **STEP 3**
- NO → Symptoms twice a month or more? — YES → Daily low dose ICS or as-needed low dose ICS-formoterol — **STEP 2**
- NO → As-needed low dose ICS-formoterol — **STEP 1**

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)
  - **Symbicort or Budeform 160/4.5 (16 puff)**

- 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 (8 inhalations of beclometasone-formoterol pMDI100/6 mcg)

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

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

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

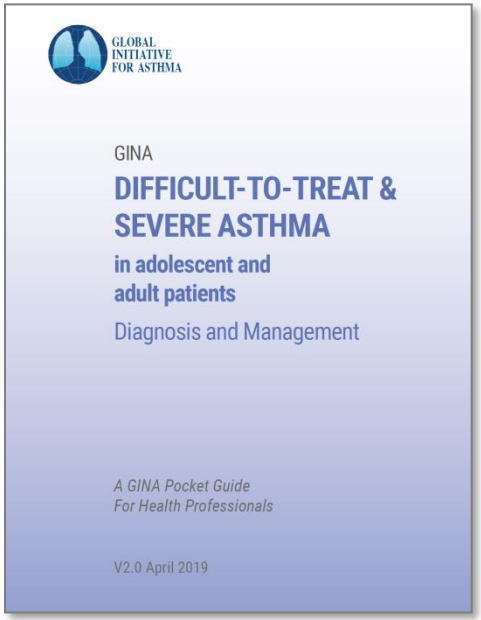
Risks may include suicidal thoughts or actions

Asthma management in children

- 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

Difficult-to-treat and severe asthma

- Pocket guide v2.0 published April 2019
- Content also included in full GINA 2020 report
- Aim is to produce a similar pocket guide for children in 2020



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

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

Other changes in GINA 2020

- Acute asthma
  - References to 'high flow oxygen' have been corrected to 'high concentration oxygen'

- 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)*

Thanks for attention

GINA Global Strategy for Asthma Management and Prevention