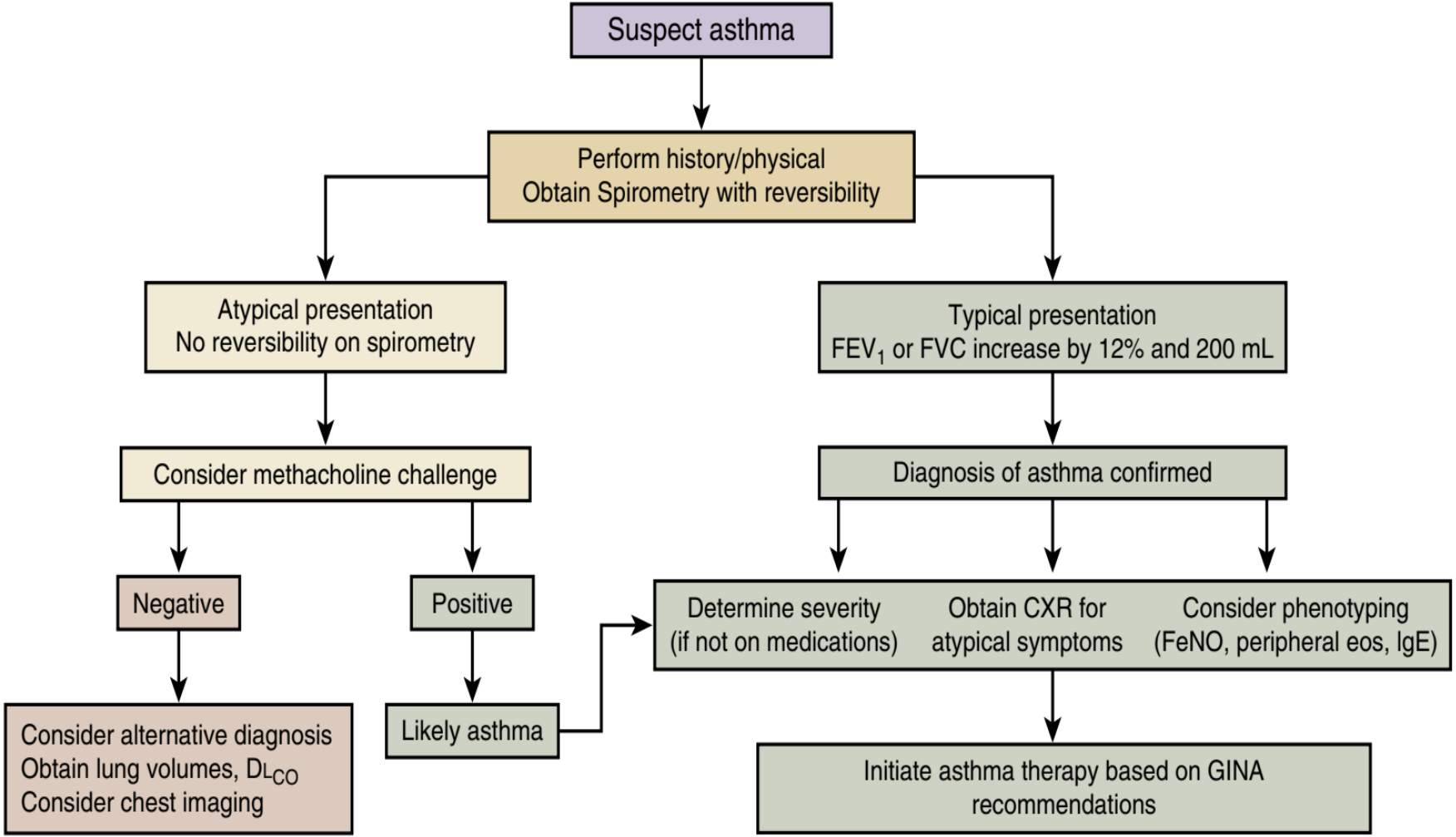

بسم الله الرحمن الرحيم

ASTHMA TREATMENT APPROACHES


Suspect asthma
Perform history/physical
Obtain Spirometry with reversibility
Atypical presentation
No reversibility on spirometry
Typical presentation
FEV1 or FVC increase by 12% and 200 mL
Consider methacholine challenge
Diagnosis of asthma confirmed
Negative
Positive
Determine severity
(if not on medications)
Obtain CXR for
atypical symptoms
Consider phenotyping
(FeNO, peripheral eos, IgE)
Consider alternative diagnosis
Obtain lung volumes, DLCO
Consider chest imaging
Likely asthma
Initiate asthma therapy based on GINA
recommendations

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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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)*
- 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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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)*

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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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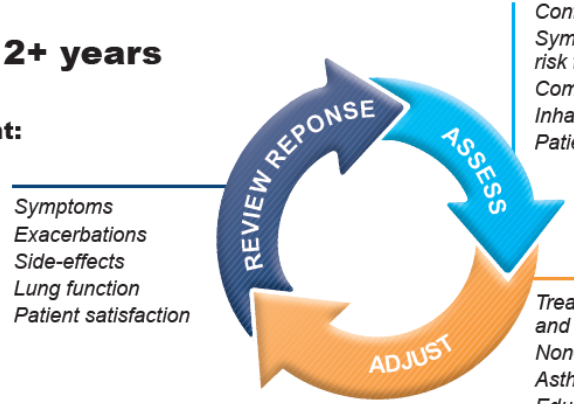
Box 3-5A

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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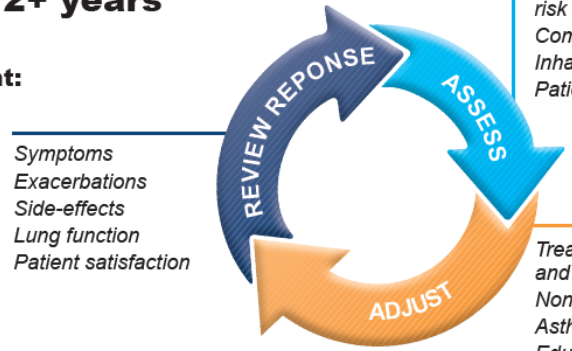

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Treatment of modifiable ris and comorbidities
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ICS-formoterol is the preferred reliever for patients prescribed maintenance and reliever therapy. For other ICS-LABAs, the reliever is SABA

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

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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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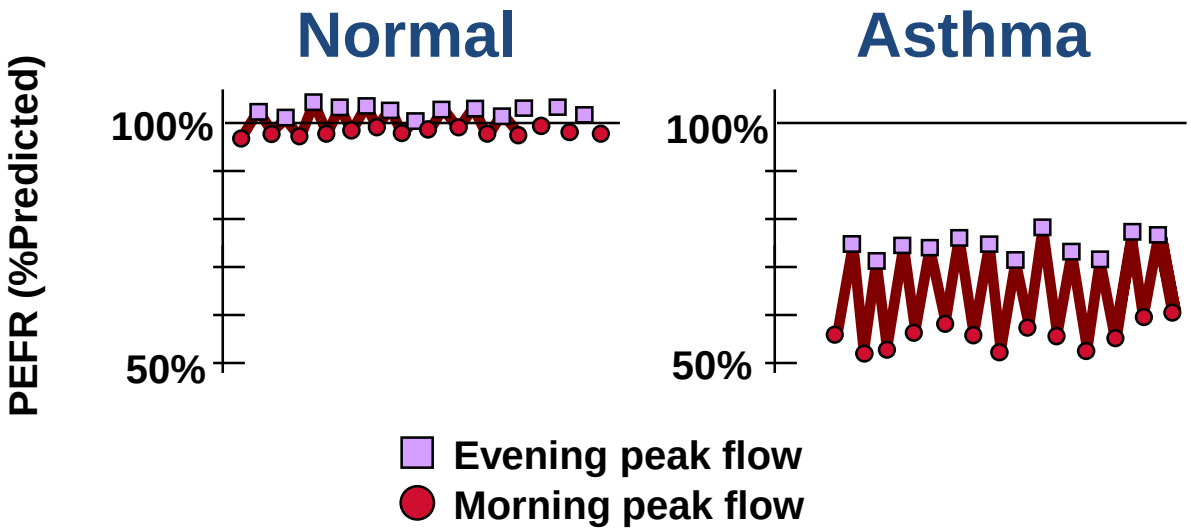
Circadian Changes in PEFR

PEFR recorded twice-daily over 2 weeks



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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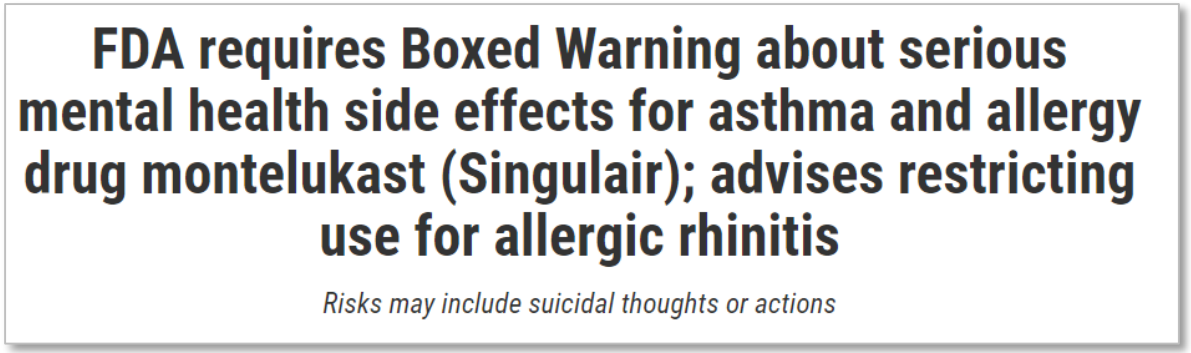
Adverse effects with montelukast

- 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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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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STEROID-SPARING THERAPIES VARIOUS IMMUNOMODULATORY TREATMENTS HAVE BEEN USED TO REDUCE THE REQUIREMENT FOR OCS IN PATIENTS WITH SEVERE ASTHMA, WHO HAVE SERIOUS SIDE EFFECTS WITH THIS THERAPY.

METHOTREXATE, CYCLOSPORIN A, AZATHIOPRINE, GOLD, AND IV GAMMAGLOBULIN HAVE ALL BEEN USED AS STEROID-SPARING THERAPIES, BUT NONE OF THESE TREATMENTS HAS ANY LONG-TERM BENEFIT AND EACH IS ASSOCIATED WITH A RELATIVELY HIGH RISK OF SIDE EFFECTS.

BRONCHIAL THERMOPLASTY BRONCHIAL THERMOPLASTY IS A BRONCHOSCOPIC TREATMENT USING THERMAL ENERGY TO ABLATE AIRWAY SMOOTH MUSCLE IN ACCESSIBLE BRONCHI.

IT MAY REDUCE EXACERBATIONS AND IMPROVE ASTHMA CONTROL IN HIGHLY SELECTED PATIENTS NOT CONTROLLED ON MAXIMAL INHALER THERAPY, PARTICULARLY WHEN THERE IS NO INCREASE IN INFLAMMATION

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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COVID-19 and asthma *(as at April 3, 2022)*

- 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

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