Breathe again, breathe again: updates in asthma

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DISCLOSURE

I have no potential conflicts of interest (COI)

Learning Objectives – Pharmacists

1. Describe the epidemiology and etiology of asthma
2. Discuss asthma treatment according to the 2020 Global Initiative for Asthma (GINA) asthma guidelines
3. Identify when to use new add on controller medications in the management of difficult to treat asthma
4. Evaluate evidence surrounding the use of tiotropium and monoclonal antibodies in the treatment of asthma

LEARNING OBJECTIVES – PHARMACY TECHNICIANS

1. Describe agents commonly used in asthma treatment according to the 2020 Global Initiative for Asthma (GINA) asthma guidelines
2. Name the anticholinergic agent and monoclonal antibodies used in the treatment of difficult to treat asthma
3. Identify the routes of administration of drugs used in difficult to treat asthma

PRE - TEST QUESTIONS - 1

Which of these medications can be used as a rescue medication for asthma according to the GINA guidelines ?

A. Fluticasone/ salmeterol

B. Budesonide/ formoterol

C. Olodaterol

D. Arformoterol

PRE - TEST QUESTIONS - 2

Which of the following can be used as a monotherapy maintenance medication for asthma according to the GINA guidelines?

A. Tiotropium

B. Salmeterol

C. Fluticasone

D. Ipratropium

PRE - TEST QUESTIONS -3

Which of these medications is an IL-4, IL-13 inhibitor?

A. Mepolizumab

B. Omalizumab

C. Dupilumab

D. Benralizumab

DEFINITION OF ASTHMA

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that can vary over time and in intensity, together with variable expiratory airflow

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

EPIDEMIOLOGY

≈ 25 million Americans have asthma

≈ 45 % of asthmatics had an asthma attack in the past 12 months

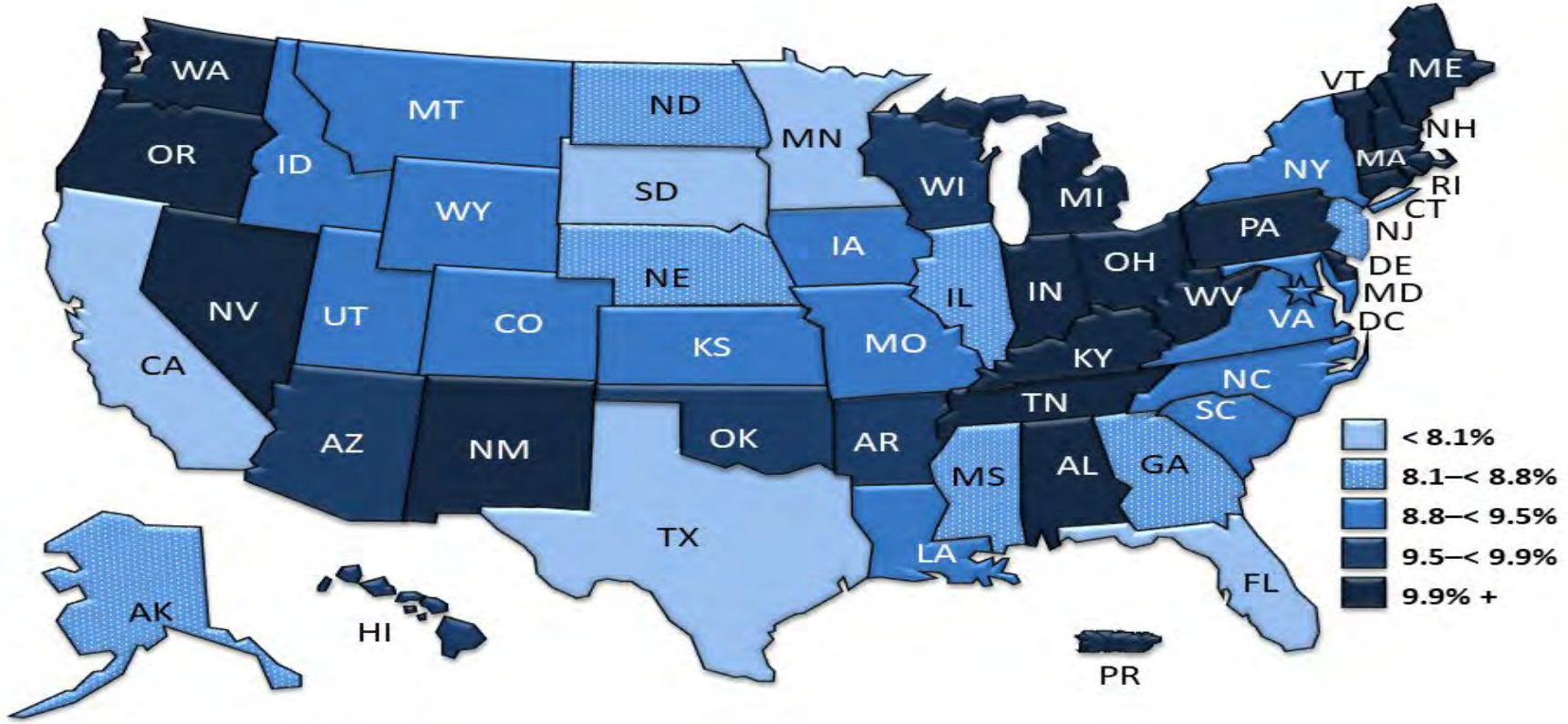
≈ 2 million ED visits annually

≈ 200,000 hospitalizations annually

> 3500 deaths

2. CDC Asthma Data, Statistics and Surveillance. 2020.

Adult Self-Reported Current Asthma Prevalence (%) by State or Territory, 2017



2. CDC Asthma Data, Statistics and Surveillance. 2020.

ETIOLOGY

Genetics vs Environmental

Likely a combination of both

Genes

Environment

- Socioeconomic status
- Family size
- Second tobacco smoke exposure
- Air pollution and allergen exposure
- Viral respiratory viruses

3. Gelfand EW. Proc Am Thorac Soc. 2009.

PATHOPHYSIOLOGY

Airway Cell Type	Inflammatory Changes
Epithelial Cells	↑ IL-33
Dendritic Cells	↑ OX40L expression, lymph node migration affecting lymphocyte maturation
Goblet Cells	Metaplasia, ↑ mucin stores
Lymphocytes	↑ TH2 bias with downregulation of Treg cells. ↑ IL-4, IL-5 and IL-13. ↑ IgE producing plasma cells
Eosinophils	IL-5 mediated accumulation
Mast cells and Basophils	↑ IgE binding and mediator storage

4. Mims JW. Int Forum Allergy Rhinol. 2015.

DIAGNOSIS

Symptoms

Detailed history

Physical examination

Spirometry

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

GOALS OF ASTHMA MANAGEMENT

1. Achieve good symptom control
2. Maintain normal activity levels
3. Minimize future risk of asthma-related mortality
4. Minimize exacerbations
5. Minimize persistent airflow limitation
6. Minimize side-effects of treatment

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

TREATMENT – DRUG CLASSES

Quick Relief Medications
Short Acting Beta Agonists (SABA), Formoterol
Anticholinergics (Short Acting)
Long-Term Control Medications
Inhaled Corticosteroids (ICS)
Long Acting Beta Agonists (LABA)
Leukotriene Modifiers
Methylxanthines
Monoclonal Antibodies
Anticholinergics* (Long Acting)

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

Bronchodilators

- Short acting beta$_2$ agonists
- Long acting beta$_2$ agonists
- Short acting muscarinic antagonists
- Long acting muscarinic antagonists

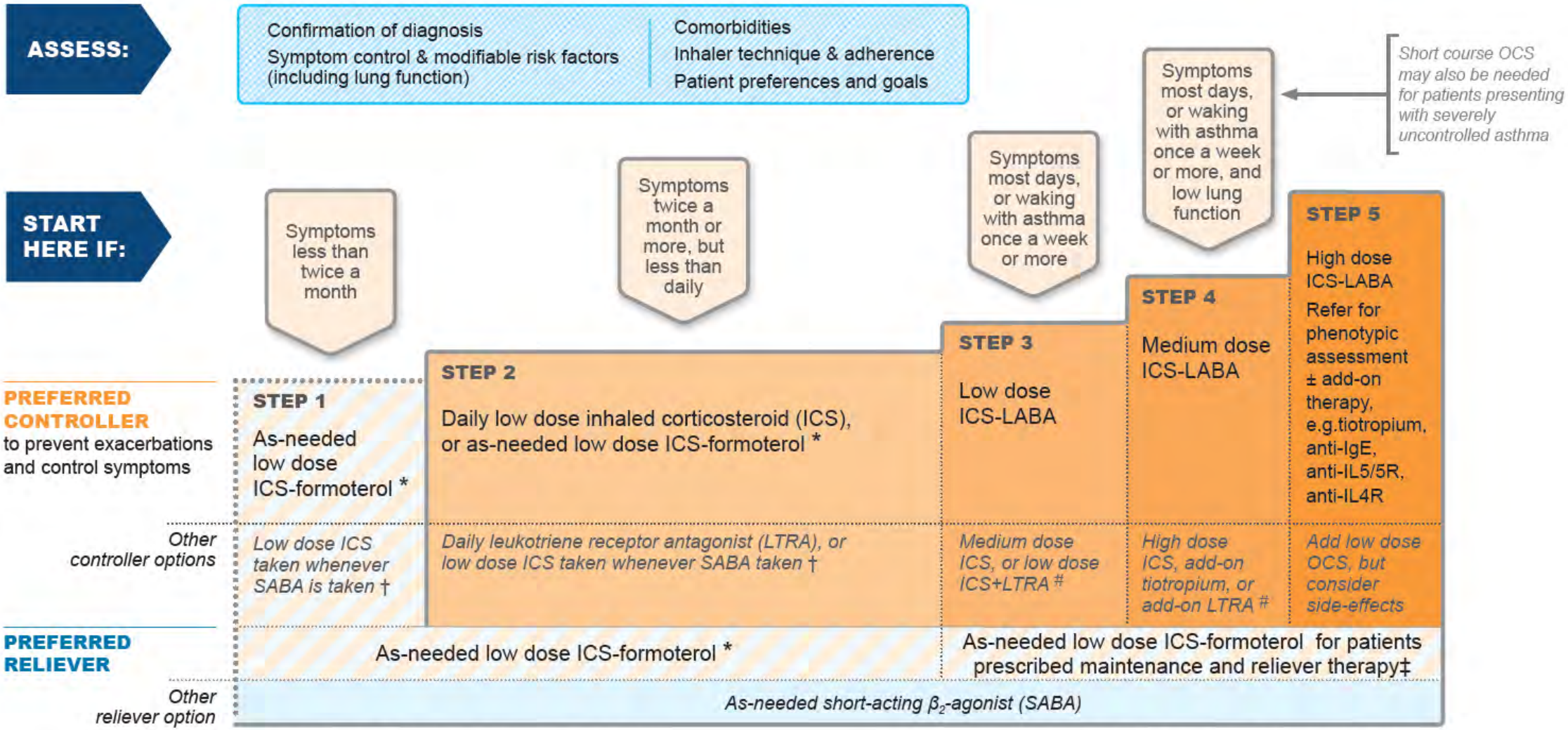
Anti-inflammatories

- Oral inhalation corticosteroids
- Leukotriene modifiers
- Monoclonal antibodies
- Methylxanthines

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

GINA GUIDELINES ALGORITHMS

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

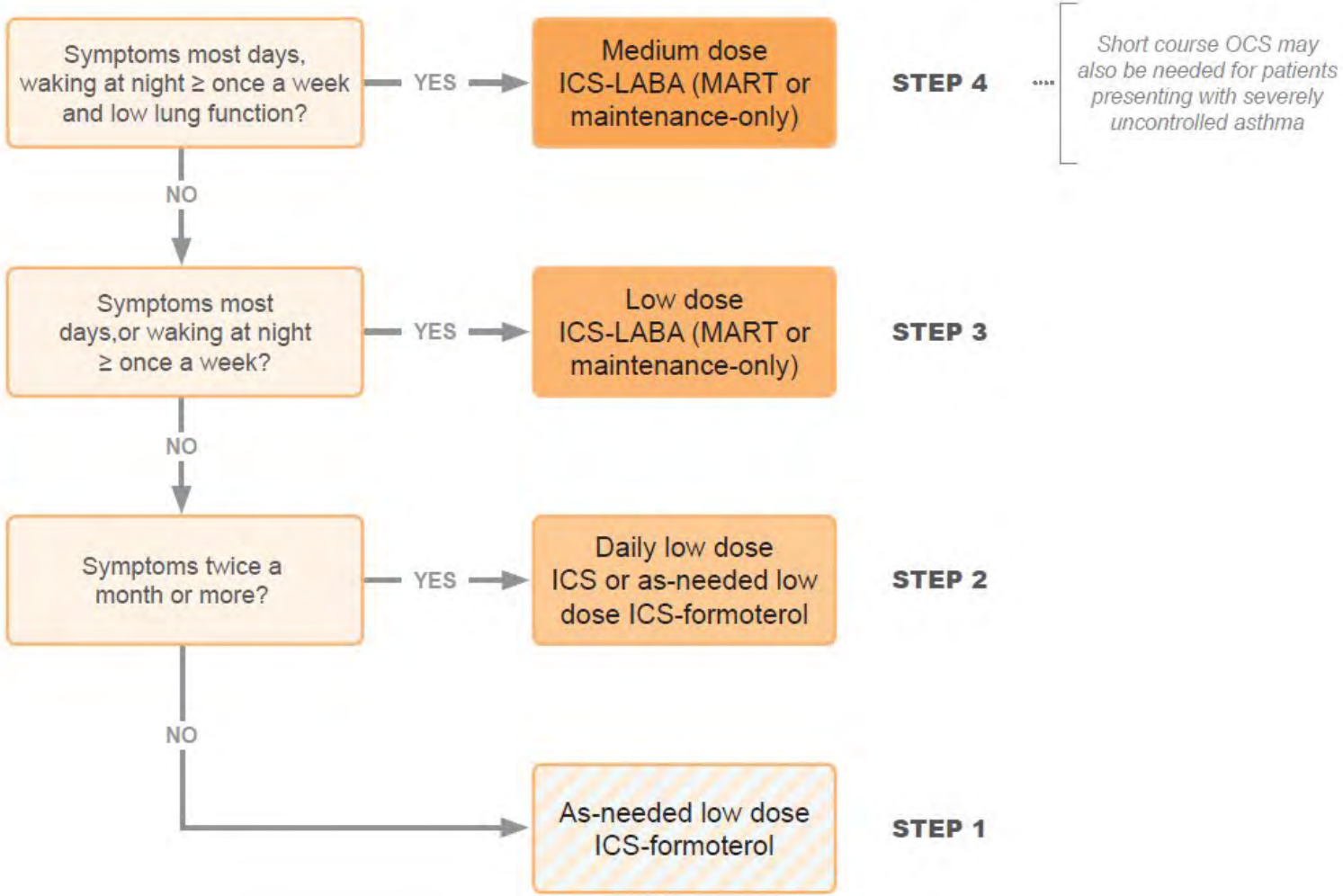
Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV1 >70% predicted

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

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



1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

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

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

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

PREFERRED CONTROLLER to prevent exacerbations and control symptoms

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
	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)

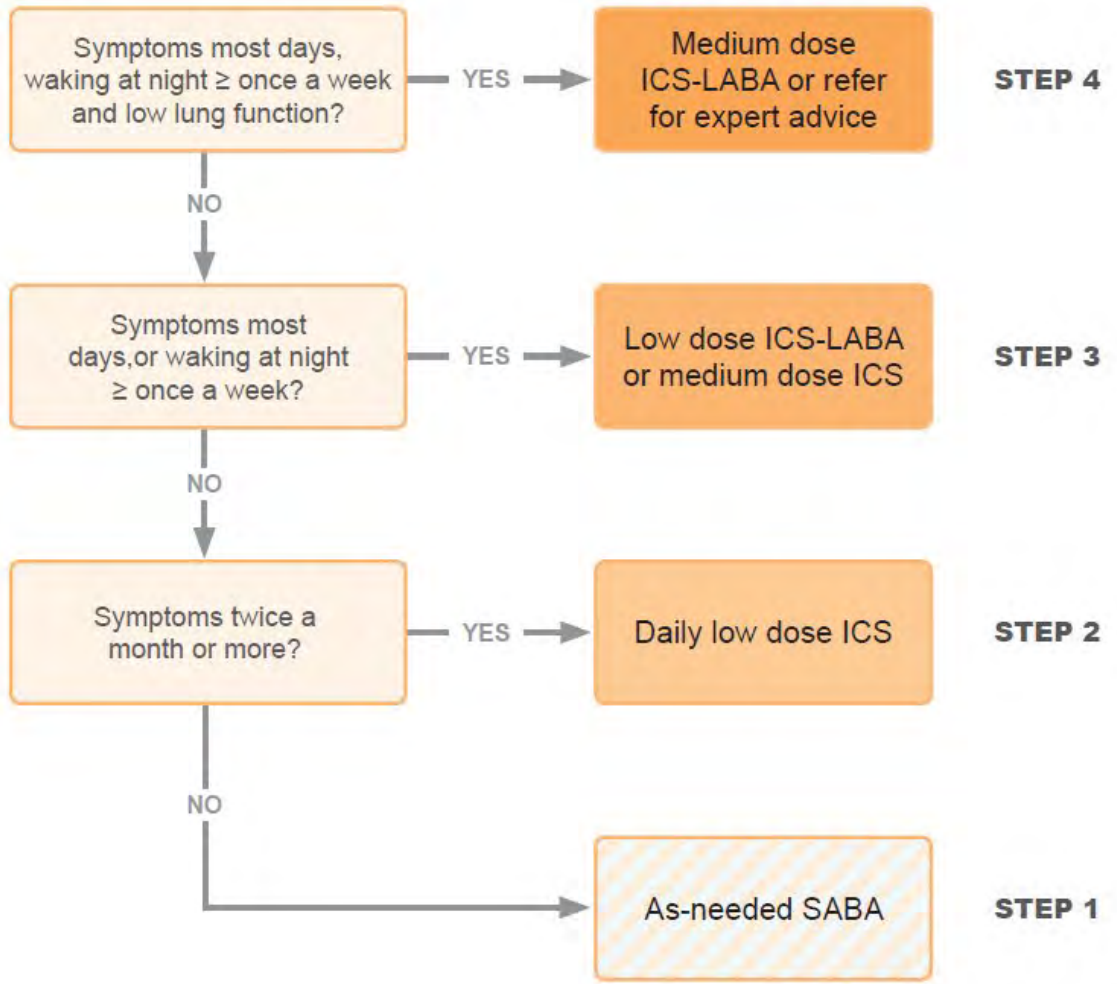
* *Separate ICS and SABA inhalers*

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

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



1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

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*

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

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*

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

GINA Treatment for Adults and Adolescents 12+ Years

	Step 1	Step 2	Step 3	Step 4	Step 5
Controller (preferred)	Low dose ICS + formoterol PRN	Low dose ICS + formoterol PRN or low dose ICS daily	Low dose ICS + LABA daily	Medium dose ICS + LABA daily	High dose ICS + LABA daily; refer for phenotype assessment and ± tiotropium, anti-IgE, anti-IL5/5R, anti-IL4
Controller (alternative)	SABA PRN + low dose ICS	LTRA daily or SABA PRN + low dose ICS	Medium dose ICS or low dose ICS + LTRA	High dose ICS + LTRA or tiotropium	Low dose oral CS
Reliever (preferred)	Low dose ICS + formoterol PRN		Low dose ICS + formoterol PRN for patients on ICS + formoterol maintenance therapy		
Reliever (alternative)	SABA PRN				

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

ICS: Inhaled corticosteroids; CS: Corticosteroids, SABA: Short Acting Beta$_2$ Agonists; LABA: Long Acting Beta$_2$ Agonists, LTRA – Leukotriene Receptor Antagonists

GINA Treatment for Children 6 to 11 years

	Step 1	Step 2	Step 3	Step 4	Step 5
Controller (preferred)	No recommendations	Low dose ICS daily	Low dose ICS + LABA daily or medium dose ICS	Medium dose ICS + LABA daily Refer for expert advice	Phenotype assessment and ±add on therapy e.g. anti-IgE
Controller (alternative option)	SABA PRN + low dose ICS	LTRA daily or SABA PRN + low dose ICS	Low dose ICS + LTRA	High dose ICS + LABA or add LTRA or tiotropium	Add anti-IL5 or low dose OCS
Reliever	SABA PRN				

ICS: Inhaled corticosteroids; CS: Corticosteroids, SABA: Short Acting Beta$_2$ Agonists; LABA: Long Acting Beta$_2$ Agonists, LTRA – Leukotriene Receptor Antagonists

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

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			
• SABA reliever for symptoms more than twice/week? • □ Yes □ No			
• Any activity limitation due to asthma? □ Yes □ No			

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

SPECIALIST CARE: SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

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

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

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

Which biologic is appropriate to start first?

Anti-IgE

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

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

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

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?

Eligible for none?
Return to section **6a**

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

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

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 ++

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

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

Good asthma response?

yes — Good response to T2-targeted therapy

unclear — Extend trial to 6-12 months

no

STOP add-on

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

no — Little/no response to T2-targeted therapy

1. GINA. Global Strategy for Asthma Management and Prevention. 2020.

DRUGS FOR DIFFICULT TO TREAT AND SEVERE ASTHMA

TIOTROPIUM (SPIRIVA®)

Dose: 2.5 mcg inh daily, can go up to 5 mcg inh daily

Class: anticholinergic, antimuscarinic

Side effects: xerostomia, upper respiratory tract infections, pharyngitis

5. Lexi-drugs. Lexi-Comp Online. 2020.

Study	Age (Years)	#	Treatment	Duration	Conclusions
Huang J et al (2016)	6-14	80	125 mcg fluticasone + placebo vs 125 mcg fluticasone + tiotropium 18 mcg DPI	12 weeks	Tiotropium group significantly improved lung function compared to placebo (FEV_1, FVC, PEF, SABA use)
Hamelmann E et al (2016)	12-17	376	ICS ± LTRA + placebo vs ICS ± LTRA + tiotropium 5 mcg or 2.5 mcg (LABA not permitted and rescue SABA allowed)	48 weeks	FEV_1 and FVC statistically improved, greatest overall benefit with 5 mcg dose
Kerstjens HA et al (2012) 2 studies combined	18-75	912	LABA/ICS + placebo vs LABA/ICS + tiotropium 5 mcg (LTRA, theophylline, oral CS, anti-IgE use permitted if stable)	48 weeks	FEV_1 and time to first exacerbation significantly improved
Kerstjens HA et al (2015) 2 studies combined	18-75	1972	ICS + placebo vs ICS + tiotropium 2.5 or 5 mcg vs ICS + salmeterol	24 weeks	Tiotropium groups significantly improved lung function (FEV_1 and PEF) and asthma control compared to placebo and has similar efficacy to salmeterol

FEV_1: Forced Expiratory Volume in 1 second, PEF: Peak Expiratory Flow; ICS: Inhaled Corticosteroids, FVC: Forced Vital Capacity; SABA: Short Acting Beta$_2$ Agonists; LTRA – Leukotriene Receptor Antagonist, LABA – Long Acting Beta$_2$ Agonists; DPI: Dry Powder Inhaler

6. Huang J. Pak J Med Sci. 2016.; 7. Hamelmann E. J Allergy Clin Immuol. 2016; 8. Kerstjens HA. N Eng J Med.2012; 9. Kerstjens HA. Lancet Respir Med. 2015

TIOTROPIUM META - ANALYSIS

13 studies; 4966 patients

Conclusions from meta –analysis

- Tiotropium is noninferior to salmeterol as add on therapy to ICS or ICS/LABA in patients with moderate to severe asthma.
- Tiotropium is superior to placebo in patients as add on therapy to ICS or ICS/LABA in patients with moderate to severe asthma.
- Tiotropium as an add on therapy to ICS/LABA showed statistically significant benefit in FEV_1 and AM and PM PEF values.

10. Rodrigo GJ. Chest. 2015.

FEV_1: Forced Expiratory Volume in 1 second, PEF: Peak Expiratory Flow

OMALIZUMAB (XOLAIR®)

Target: IgE

Dose: 75 – 375 mcg subQ q 2 to 4 weeks

Population to consider: ≥ 6years, severe allergic asthma; serum IgE 30 IU/mL; + skin test or in vitro reactivity to perennial aeroallergens; symptoms inadequately controlled with ICS

Observed clinical effects: ↓exacerbations; modest ↓reduction in symptoms; modest ↑ in lung function

5. Lexi-drugs. Lexi-Comp Online. 2020; 11. Israel E. N Eng J Med. 2017

ICS: Inhaled Corticosteroid

OMALIZUMAB META - ANALYSIS

6 studies; 2949 patients

Efficacy results that statistically favor omalizumab

- Exacerbation rate
- GETE
- AQLQ

GETE: Global Evaluation of Treatment Effectiveness, AQLQ: Asthma Quality of Life Questionnaire

12. Lai T. Sci Rep. 2015.

BENRALIZUMAB (FASENRA®)

Target: IL-5

Dose: 30 mcg subQ q 4 weeks X 3 doses, then q 8 weeks*

Population to consider: ≥ 12 years; severe asthma; serum eosinophils 300 cells/µL

Observed clinical effects: ↓exacerbations; ↓reduction in symptoms; modest ↑in lung function

5. Lexi-drugs. Lexi-Comp Online. 2020; 11. Israel E. N Eng J Med. 2017

* Can be self-administered at home

BENRALIZUMAB META - ANALYSIS

5 studies; 1951 patients

Efficacy results that statistically favor benralizumab

- FEV_1
- AQLQ
- Exacerbation rate
- ACQ-6

FEV_1: Forced Expiratory Volume in 1 second, AQLQ: Asthma Quality of Life Questionnaire, ACQ: Asthma Control Questionnaire

13. Liu T. Front Med. 2018.

RESLIZUMAB (CINQAIR®)

Target: IL-5

Dose: 3 mg/kg IV q 4 weeks

Population to consider: ≥ 18 years; severe asthma; serum eosinophils 400 cells/µL

Observed clinical effects: ↓exacerbations; ↓reduction in symptoms; modest ↑in lung function

5. Lexi-drugs. Lexi-Comp Online. 2020; 11. Israel E. N Eng J Med. 2017

RESLIZUMAB META - ANALYSIS

5 studies; 1347 patients

Efficacy results that statistically favor reslizumab

- FEV_1
- ACQ-7
- FVC
- ASUI
- Blood eosinophil count
- Change in frequency of rescue use of SABA
- AQLQ

14. Milosavljevic MN. Vojnosanit Pregl. 2018.

FEV_1: Forced Expiratory Volume in 1 second, AQLQ: Asthma Quality of Life Questionnaire, ACQ: Asthma Control Questionnaire, ASUI: Asthma Symptom Utility Index, FVC: Forced Vital Capacity

MEPOLIZUMAB (NUCALA®)

Target: IL-5

Dose: 100 mg subQ q 4 weeks*

Population to consider: ≥ 12 years; severe asthma; serum eosinophils 150 – 300 cells/µL

Observed clinical effects: ↓exacerbations; ↓reduction in symptoms; modest ↑in lung function

5. Lexi-drugs. Lexi-Comp Online. 2020; 11. Israel E. N Eng J Med. 2017

* Can be self-administered at home

MEPOLIZUMAB META - ANALYSIS

5 studies; 3369 patients

Efficacy results that statistically favor mepolizumab

- Annual exacerbation rate
- FEV_1
- ACQ-5
- SGRQ
- Blood eosinophil counts

15. Albers FC. Respir Res. 2019.

FEV_1: Forced Expiratory Volume in 1 second, SGRQ: St. George's Respiratory Questionnaire, ACQ: Asthma Control Questionnaire

DUPILUMAB (DUPIXENT®)

Target: IL-4 and IL-13

Dose: 400 or 600 mg subQ (loading dose) then 200 or 300 mg subQ q other week*

Population to consider: ≥ 12 years; severe asthma; oral corticosteroid dependent; serum eosinophils 300 cells/µL

Observed clinical effects: ↓exacerbations; ↑in lung function

5. Lexi-drugs. Lexi-Comp Online. 2020; 11. Israel E. N Eng J Med. 2017

* Can be self-administered at home

DUPILUMAB META - ANALYSIS

5 studies; 3369 patients

Efficacy results that statistically favor dupilumab

- FEV_1
- ACQ-5
- FE_{NO}
- AM and PM asthma symptom control
- Exacerbation rate
- AQLQ

16. Xiong X. Respir Res. 2019.

FEV_1: Forced Expiratory Volume in 1 second, AQLQ: Asthma Quality of Life Questionnaire, ACQ: Asthma Control Questionnaire, FE_{NO}: Fractional Exhaled Nitric Oxide

COMPARISON OF BIOLOGIC AGENTS – EFFICACY

Biologic Agent	Asthma Exacerbations Requiring Steroids Risk Ratio (95% CI)	Mean Difference in Pre Bronchodilator FEV1 vs Placebo (95% CI)	Mean Difference in AQLQ vs Placebo (95% CI)	Mean Difference in ACQ vs Placebo (95% CI)
Omalizumab	0.52 (0.37-0.73)	0.06 (0.02-0.10)	0.26 (0.05-0.47)	NR
Mepolizumab	0.45 (0.36-0.55)	0.10 (0.01-0.18)	0.35 (0.08-0.62)	-0.42 (-0.56 to -0.28)
Reslizumab	0.43 (0.33-0.55)	0.12 (0.08-0.16)	0.28 (0.17-0.39)	-0.27 (-0.36 to -0.15)
Benralizumab	0.59 (0.51-0.68)	0.13 (0.08-0.19)	0.23 (0.11-0.35)	-0.23 (-0.34 to -0.12)
Dupilumab 200 mg	0.52 (0.41-0.66)	0.14 (0.08-0.19)	0.29 (0.15-0.44)	-0.39 (-0.53 to -0.25)
Dupilumab 300 mg	0.54 (0.43-0.68)	0.13 (0.08-0.18)	0.26 (0.12-0.40)	-0.22 (-0.36 to -0.08)

17. Tice J et al. ICER Review. 2018.

COMPARISON OF BIOLOGIC AGENTS – SAFETY

Biologic Agent	Serious Adverse Effects Risk Ratio (95% CI)	Adverse Events Leading to Drug Discontinuation Risk Ratio (95% CI)	Injection Site Reactions Risk Ratio (95% CI)
Omalizumab	0.72 (0.57-0.91)	1.41 (0.84-2.37)	1.72 (1.33-2.24)
Mepolizumab	0.63 (0.41-0.97)	0.45 (0.11-1.80)	1.98 (1.06-3.72)
Reslizumab	0.79 (0.51-1.22)	0.67 (0.37-1.20)	0.62 (0.20-1.89)
Benralizumab	0.80 (0.60-1.06)	2.70 (0.80-8.49)	1.43 (0.81-2.52)
Dupilumab 200 mg	0.93 (0.59-1.47)	0.50 (0.27-0.92)	2.80 (1.70-4.61)
Dupilumab 300 mg	1.03 (0.67-1.61)	2.23 (1.14-4.38)	1.79 (1.24-4.38)

17. Tice J. ICER Review. 2018.

SIDE EFFECTS OF MONOCLONAL ANTIBODIES

Anaphylaxis

Injection site reactions

Helminth infections

5. Lexi-drugs. Lexi-Comp Online. 2020.

ROLE OF A PHARMACIST

1. Identify patients with poorly controlled asthma
2. Monitor medication use and refill intervals
3. Educate patients about asthma medications
4. Instruct patients about correct technique for using inhaled products
5. Help patients use peak flow meters correctly
6. Encourage patients using OTC inhalers and asthma medications to seek medical help
7. Ensure patients understands their asthma action plan
8. Encourage allergen avoidance

GINA COVID – 19 STATEMENT

Nebulizers should be avoided if possible due to risk of disseminating COVID-19

Pressurized metered dose inhalers (pMDI) via a spacer is the preferred treatment during severe attacks

Maintenance treatment should be continued if patient is being treated for a severe attack

Routine spirometry testing should be suspended at this time

18. GINA. COVID 19. 2020.

POST - TEST QUESTIONS -1

Which of these medications can be used as a rescue medication for asthma according to the GINA guidelines ?

A. Fluticasone/ salmeterol

B. Budesonide/ formoterol

C. Olodaterol

D. Arformoterol

PRE - TEST QUESTIONS - 2

Which of the following can be used as a monotherapy maintenance medication for asthma according to the GINA guidelines?

A. Tiotropium

B. Salmeterol

C. Fluticasone

D. Ipratropium

POST - TEST QUESTIONS - 3

Which of these medications is an IL-4, IL-13 inhibitor?

A. Mepolizumab

B. Omalizumab

C. Dupilumab

D. Benralizumab

REFERENCE LIST

1. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. Posted 2020.doi: https://ginasthma.org/wp-content/uploads/2020/04/GINA-2020-full-report_-final-_wms.pdf. Updated 2020. Accessed July 10, 2020.
2. Centers for Disease Control and Prevention. Asthma Data, Statistics and Surveillance. Updated 2020. doi. https://www.cdc.gov/asthma/asthmadata.htm. Accessed July 10, 2020.
3. Gelfand EW. Pediatric Asthma: A Different Disease. Proc Am Thorac Soc. 2009;6(3):278-282. Posted 2009. doi:10.1513/pats.200808-090RM. Accessed July 10, 2020.
4. Mims JW. Asthma: Definitions and Pathophysiology. Int Forum Allergy Rhinol. 2015;5 Suppl 1:S2-S6. Posted 2015. doi:10.1002/alr.21609. Accessed July 10, 2020.
5. LexiComp Online, Lexi-Drugs, Hudson, OH. Available at: http://online.lexi.com.roseman.idm.oclc.org/lco/action/home. Accessed July 12, 2020.
6. Huang J, Chen Y, Long Z, Zhou X, et al. Clinical Efficacy of Tiotropium in Children with Asthma. Pak J Med Sci. 2016;32(2):462-465. Posted 2016. doi:10.12669/pjms.322.8836. Accessed July 12, 2020.
7. Hamelmann E, Bateman ED, Vogelberg C, et al. Tiotropium Add-on Therapy in Adolescents with Moderate Asthma: A 1-year Randomized Controlled Trial. J Allergy Clin Immunol. 2016;138(2):441-450.e8. Posted 2016. doi:10.1016/j.jaci.2016.01.011. Accessed July 12, 2020.
8. Kerstjens HA, Engel M, Dahl R, et al. Tiotropium in Asthma Poorly Controlled with Standard Combination Therapy. N Engl J Med. 2012;367(13):1198-1207. Posted 2012. doi:10.1056/NEJMoa1208606. Accessed July 12, 2020.
9. Kerstjens HA, Casale TB, Bleecker ER, et al. Tiotropium or Salmeterol as Add-on Therapy to Inhaled Corticosteroids for Patients with Moderate Symptomatic Asthma: Two Replicate, Double-blind, Placebo-controlled, Parallel-group, Active-comparator, Randomised Trials. Lancet Respir Med. 2015;3(5):367-376. Posted 2015. doi:10.1016/S2213-2600(15)00031-4. Accessed July 12, 2020.
10. Rodrigo GJ, Castro-Rodríguez JA. What is the Role of Tiotropium in Asthma?: A Systematic Review with Meta-analysis. Chest. 2015;147(2): 388-396. Posted 2015, doi. https://doi.org/10.1378/chest.14-1698. Accessed July 10, 2020.

REFERENCE LIST

11. Israel E, Reddel HK. Severe and Difficult-to-Treat Asthma in Adults. N Engl J Med. 2017;377(10):965-976. Posted 2017. doi:10.1056/NEJMra1608969. Accessed July 16, 2020.

12. Lai T, Wang S, Xu Z, et al. Long-term Efficacy and Safety of Omalizumab in Patients with Persistent Uncontrolled Allergic Asthma: A Systematic Review and Meta-analysis. *Sci Rep*. 2015:*5(*8191). https://doi.org/10.1038/srep08191. Accessed July 16, 2020.

13. Liu T, Wang F, Wang G. et al. Efficacy and Safety of Benralizumab in Patients with Eosinophilic Asthma: A Meta-analysis of Randomized Placebo-controlled Trials. Front. Med. 2018;12:340–349. Posted 2018. https://doi.org/10.1007/s11684-017-0565-0. Accessed July 16,2020.

14. Milosavljevic MN, Jankovic SM, Pejcic AV, et al. Vojnosanit Pregl. 2018;75(9):884-896. Posted 2018. doi:https://scidar.kg.ac.rs/bitstream/123456789/8154/1/10.2298-VSP161124013M.pdf. Accessed July 16, 2020.

15. Albers FC, Papi A, Taillé C, et al. Mepolizumab Reduces Exacerbations in Patients with Severe Eosinophilic Asthma, Irrespective of Body Weight/Body Mass Index: Meta-analysis of MENSA and MUSCA. Respir Res. 2019; 20(169):1134-1137. Posted 2019. https://doi.org/10.1186/s12931-019-1134-7. Accessed July 16, 2020.

16. Xiong XF, Zhu M, Wu HX, et al. Efficacy and Safety of Dupilumab For the Treatment of Uncontrolled Asthma: A Meta-analysis of Randomized Clinical Trials. Respir Res. 2019;20(1):108. Posted 2019. doi:10.1186/s12931-019-1065-3. Accessed July 16, 2020.

17. Tice JA, Walsh JME, Synnott P, et al. Biologic Therapies for Treatment of Asthma Associated with Type 2 Inflammation: Effectiveness, Value, and Value-based Price Benchmarks. 2018. Institute for Clinical and Economic Review. doi: https://icer-review.org/wp-content/uploads/2018/04/ICER_Asthma_Draft_Report_092418v1.pdf. Accessed July 17, 2020.

18. Global Initiative for Asthma (GINA). COVID-19: GINA Answers to Frequently Asked Questions on Asthma Management. Posted 2020.doi: https://ginasthma.org/covid-19-gina-answers-to-frequently-asked-questions-on-asthma-management/. Accessed July 18, 2020.

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