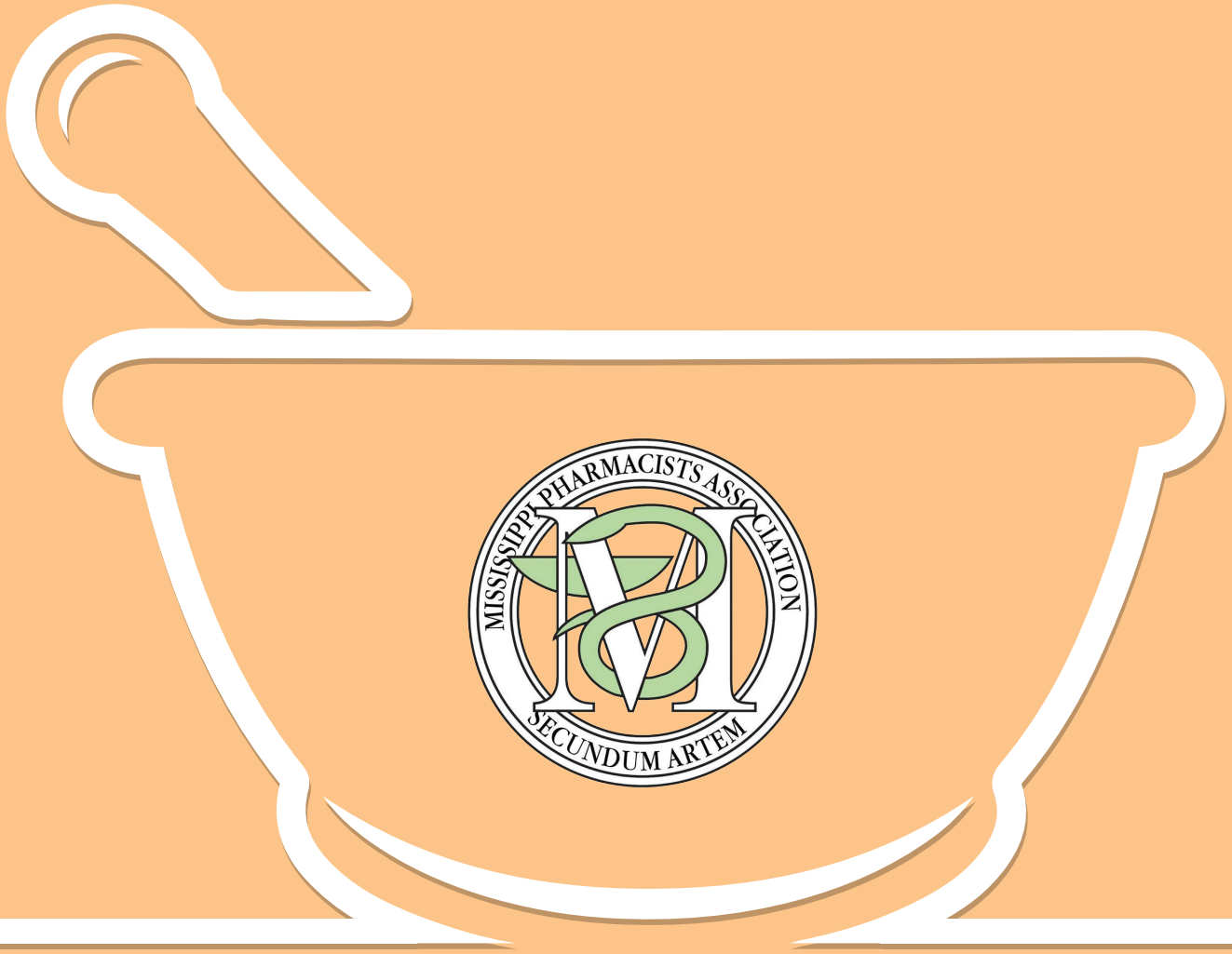
Mississippi Pharmacist

Quarterly publication of the Mississippi Pharmacists Association | Fall 2020



Wes Pitts,
MPhA President
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This emblem designates *Mississippi Pharmacist* is a member of the State Pharmaceutical Editorial Association, recognizing its high journalistic standards in endeavoring to keep its members well informed on all developments relative to the pharmaceutical profession.

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PRESIDENT'S NOTE

Dear MPhA Members,

As we enter the dog days of summer and the heat of election season, it comes to mind how important it is being vocal and active in the legislative process. There are a number of ways you can help your patients, our profession, and MPhA in the political arena.

One way is to make sure you know who your representatives and senators are on the state and national level. If you haven't done so, please take time to learn who your legislators are. Reach out to them to thank them for their service and educate them about the important roles a pharmacist can play on the healthcare team to improve outcomes and control costs. If you do not know who your elected officials are, you can learn by visiting https://openstates.org/ where you can search for your legislators by your address.

Another very important way you can contribute to the advancement of the pharmacy profession is to support the MPhA Political Action Committee (PAC). If you were not aware, a PAC is an organization that that collects campaign contributions from members and donates those funds to campaigns for or against candidates, ballot initiatives, or legislation. Your support of the MPhA PAC allows us to educate senators and representatives about the important work pharmacists do in all healthcare settings. This is more important than ever as we urge the Mississippi Legislature to take action on critical issues facing the healthcare system such as patients' access to services of pharmacists, the rising cost of medications, and roadblocks that prevent pharmacists from practicing at the highest level of their licensure. A well-funded PAC will help:

- Protect your patients by helping your members of the Mississippi Legislature understand the issues that you face and pass laws that will support your role.
- Elect members of the Mississippi Legislature who support the role of pharmacists in patient care.
- Build relationships in the Mississippi Legislature and educate legislators about our issues.

You can contribute to the PAC by visiting https://www.mspharm.org/copy-of-ms-pharm-pac and choosing to make a recurring or one-time donation. We recently sent communication with a suggestion for $20 per month. If everyone contributes even a small amount, we can ensure that we do have a well-funded PAC to help achieve our goals. As the Kenyan proverb says, "Sticks in a bundle are unbreakable."

Please let us know how we can help you or if you would like to get more involved with MPhA.

Sincerely yours,

Wes Pitts, Pharm.D., BCPS, FASHP, FMSHP

MPhA President

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The Magnolia State Pharmaceutical Society (MSPS) is a pharmacy organization that was founded in Mississippi in the early 1960s by minority pharmacists. MSPS is the Mississippi Chapter of the National Pharmaceutical Association (NPhA), founded in 1947 by Dr. Chauncey I. Cooper. The founding of these organizations was in response to a need for national and local organizations committed to serve the underserved, improve the healthcare disparities of minority communities, and promote minorities in the profession of pharmacy. The pharmacist and technician members practice in a variety of areas of pharmacy, including but not limited to health systems, community, independents, long-term care, managed care and academia.

Since inception, the members of MSPS have participated in various initiatives that support the pharmacy community and the community at large. Members regularly provide medication counseling, blood pressure checks and chronic disease education at community health fairs, serve as career day panelists, and serve as subject matter experts on various community committees. MSPS also works to give back to the profession and the state by assisting in the recruitment of the best and brightest high school and college students to Mississippi schools of pharmacy. In addition, MSPS supports the members and programs of the pharmacy school student affiliate organization, Student National Pharmaceutical Association (SNPhA). Some efforts include hosting networking opportunities for students to meet pharmacists and participating in cultural activities alongside students.

The most recent initiative for MSPS is participation in Civic Health Month for August 2020. As noted on the website (www.civichealthmonth.org), Civic Health Month is a collaboration between health organizations that support civic engagement, voter registration nonprofits that support health care and individual healthcare providers passionate about civic engagement. Locally, MSPS will be participating in a drive thru community service event that will include a school supplies give away, voter registration, and census completion assistance.

Please take a second to visit us at https://www.facebook.com/MagnoliaStatePharmaceuticalSociety/.

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EXECUTIVE DIRECTOR'S MESSAGE

MPhA Executive Director's Letter Q3 2020

2020, right? As I'm writing this, there is the potential for 2 hurricanes in the Gulf of Mexico for the first time in recorded history and an asteroid is headed toward earth that may enter our atmosphere in November. Luckily the asteroid is too small to destroy the earth and the hurricanes are not expected to combine to form a Super Hurricane.

But if you're looking for some good news in 2020, you currently have the right journal in your hands. MPhA is doing great things in 2020. Our membership is continually increasing along with our PAC donations, we have had a successful virtual convention with an amazing 170 attendees, we have had a very successful legislative session, and are looking forward to a successful Consultant Seminar and Last Chance Seminar.

There are five pharmacy associations in Mississippi; Mississippi Pharmacists Association (MPhA), Mississippi Society of Health-Systems Pharmacists (MSHP), Mississippi Independent Pharmacies Association (MIPA), Magnolia State Pharmaceutical Society (MSPS), and Mississippi College of Clinical Pharmacists (MCCP). These associations are all doing a lot of great work for our profession in the state. Of the five, MPhA is the association that represents all pharmacists across the state and works in cooperation with the other four associations on many issues affecting our profession. This has been an amazing year with the associations working together on issues concerning COVID-19 and supporting MIPA's work on HB 708.

In the next few journals, we are going to spotlight these other associations. I would venture to say that many pharmacists in MS don't know that we have five associations or each of their specialties. We will begin in this journal with the Magnolia State Pharmaceutical Society. The current president, Jameika Stuckey, has been kind enough to give us an overview and history of MSPS. Jameika is an awesome person and pharmacist and I'm thankful to call her a friend!

I want to thank our committee chairs and members who are volunteering their time and doing a wonderful job making MPhA successful this year. I encourage anyone not involved to get involved and help promote and strengthen our great profession.

Thank you,

Beau Cox

Schedule:

8:00 - 9:30	CAPping off the year: updates and changes to the recommendations for community-acquired pneumonia (Kayla Stover)
9:30 - 10:30	Transplant Medications – OUT with the OLD and IN with the NEW (Alicia Patel)
10:30 - 12:00	Clinical Pearls for Pharmacists (Buddy Ogletree)
12:00 - 1:00	BREAK
1:00 - 2:00	Electrolyte Management Principles for the Pharmacist (Phil Ayers)
2:00 - 3:00	COVID-19 (Coronavirus): Mississippi Long-Term Care Facilities (Anna Kathryn Ward)
3:00 - 4:00	Consultant Pharmacy Law Update 2020 (Randy Pittman)
4:00 - 5:00	Benzodiazepine Use in Geriatrics (Jennifer Duncan)

Register at mspharm.org or Call (601) 981-0416

WHAT'S NEW IN THE TREATMENT OF ASTHMA? AN UPDATE TO THE GUIDELINES

TJ Smith, PharmD, Assistant Professor of Pharmacy Practice, William Carey University School of Pharmacy; Donna Adkins, PharmD, BCGP, Professor and Chair, Department of Pharmacy Practice, William Carey School of Pharmacy; Charles Breese, PhD, Professor of Pharmacology and Associate Dean of Curriculum and Student Success, William Carey University School of Pharmacy.

Special thanks to the Global Initiative for Asthma for granting permission to use the stepwise treatment recommendations referenced in this article.

Asthma is a chronic, incurable disease of the lungs in which the patient suffers from wheezing, coughing, and shortness of breath resulting in airflow limitation. It estimated that 26 million people in the United States have asthma. In Mississippi, 13% of children aged 0-17 years have asthma, many of which have poor control over their symptoms[2].

The Global Initiative for Asthma (GINA) is published annually and serves as a reliable resource for healthcare professionals when diagnosing, treating, and monitoring the asthmatic patient's therapeutic regimen[1].

Key Summary Points – Controllers
Review of available asthmatic medication pharmacology:

Diagnosis and pharmacotherapy for asthma in the US has largely been driven by the Expert Panel Report-3 Guidelines for the Diagnosis and Management of Asthma(EPR-3), in which increasing levels of pharmacotherapy are utilized based on the severity of the asthma (or "Step")[3]. As discussed later, changes to the management of asthma, particularly mild asthma[3,4], has been recommended by the Global Initiative for Asthma[5,1]. In addition, the availability of targeted monoclonal antibodies may further revolutionize the management of patients with severe asthma. Below, each of the general classes of medications used in asthma are reviewed and summarized[6]. Short acting beta-2 agonists (SABA) relax bronchial airways smooth muscle via activation of β2 receptors and increases airflow in as little as 2-5 minutes. Short acting beta-2 agonists have long been considered the drug of choice for treating emergent symptoms. Everyone with respiratory disease (asthma or COPD) should have an albuterol rescue inhaler. Albuterol (Ventolin, Proventil) is considered the gold standard β-agonist agent, which is a racemic mixture available for oral and inhalation therapies[7]. Levalbuterol (Xopenex) is the R-enantiomer of albuterol and is available as an inhaler and nebulized solution[8]. Studies indicate that both agents have similar effects and safety profiles[9]. The adverse reactions are largely mediated by beta-1 activity on the cardiovascular system, and fewer side effects are seen with proper use. The most common side effects include restlessness and apprehension, tachycardia, fine muscle tremor, and anxiety. As an inhaled therapy, patients will typically see a rapid onset of action with fewer systemic side effects. Use of 1 canister per month indicates inadequate control and the need to intensify anti-inflammatory therapy. SABAs are generally used on an as needed (PRN) schedule[10,11].

"Controller" or anti-inflammatory medications include several classes of medications, including inhaled glucocorticosteroids, oral glucocorticosteroids, the leukotriene receptor antagonists and enzyme inhibitor and the long-acting inhaled ß2-agonist[6]. The agents are used to gain long-term control of asthma and reduce exacerbations associated with poor asthma control[10,11]. The inhaled glucocorticosteroids are considered the preferred treatment alone or in combination with other controller medications for all persistent categories of asthma. There are numerous products available and the doses are dependent on the product and delivery device[11]. Inhaled glucocorticosteroids are typically used every day or twice a day for mild persistent asthma. BID therapy is typically more common in moderate-to-severe persistent asthma[11]. Inhaled glucocorticosteroids are potent and safe when use is monitored and reduces asthma symptoms, exacerbations, bronchial hyper reactivity, hospitalizations, and improves spirometry measures[12]. Inhaled glucocorticosteroids may also prevent airways remodeling. Steroids primarily exert their effects by binding to glucocorticoid receptors to regulate gene transcription within target cells. Glucocorticosteroids inhibit the inflammatory response in asthma by inhibiting the Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-kB) and Activator Protein 1 (AP-1 is a transcription factor that regulates gene expression activity), suppresses the production and secretion of cytokines, chemokines, cell adhesion molecules by the airway epithelium, and decreases the numbers of eosinophils and lymphocytes. Furthermore, glucocorticoids inhibit production of prostaglandins and leukotrienes (which mediate inflammation). This occurs via inhibiting phospholipase A2, which is needed for prostaglandins synthesis. Glucocorticosteroids also decrease inflammation by decreasing permeability of capillary membranes, reducing swelling, and reducing the effects of histamine[12,13].

The use of oral glucocorticosteroids, such as prednisone or prednisolone are primarily used to either acutely speed resolution of airflow obstruction, or chronically to reduce the rate of relapse in patients with severe asthma. Systemic steroids may help gain prompt control of disease when initiating inhaled treatment and in severe-persistent asthma that is not controlled by other means. Oral glucocorticosteroids have more significant side-effect profile as compared to inhaled steroid agents and patients should be closely monitored for emergent side effects as described below[11].

One of the more common side effects of inhaled Corticosteroids (ICSs) includes the deposition of the steroid in mouth and throat which may promote oral candidiasis, which appears as a white coating in the mouth. This may be prevented by rinsing

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the mouth with water after use, which should be a major counseling point of pharmacists[11]. Short-term steroid use, mostly seen with systemic use, includes reversible increases in plasma glucose, decreases in serum potassium, fluid retention with weight gain, mood alterations including rare psychosis, hypertension, and peptic ulcers. Long-term systemic steroid use can be associated with more serious side effects such as height and growth suppression, immune suppression, cataracts, hirsutism, hypertension, and steroid dependence. Cases of iatrogenic Cushing's syndrome have been reported if use is not appropriately monitored. In addition, the use of oral glucocorticosteroids should always be tapered in order to avoid hypothalamic pituitary axis (HPA) suppression leading to iatrogenic Addison's syndrome[10,11].

The next class of controller medications are the long-acting beta-2 agonists, which include salmeterol, formoterol, and arformoterol. In asthma patients, long-acting beta-2 agonists are used concomitantly with anti-inflammatory medications for long-term symptom control and should not be used PRN[11]. Long-acting beta-2 agonists are especially helpful with nocturnal symptoms and can help prevent exercise-induced bronchospasms. Salmeterol has a longer onset of action (≈15-30 minutes) and should not be used for emerging symptoms. Formoterol appears to have more rapid onset of action, similar to that of albuterol. The duration of action of these medications is about 12 hours. Long-acting beta-2 agonists for asthmatic patients are sold as combination products to improve compliance in patients with asthma. Arformoterol (Brovana) is also available as solution for nebulizer. More recently, longer-acting beta-agonists or 'Ultra-LABAs' have become available with a 24-hour duration of action and once-daily dosing. While these agents are currently approved for COPD, vilanterol in combination with Fluticasone (Breo Ellipta) has been approved for use in asthma. Other Ultra-LABAs include Indacaterol (Arcapta Neohaler) and olodaterol (Striverdi® Respimat®)[10,11,14].

Parasympathetic cholinergic innervation is important in the regulation of airways smooth muscle tone, with increases in cholinergic tone causing bronchoconstriction and increased secretions. This vagally derived innervation extends along the length of the bronchial tree, but predominates in large and medium-sized airways. Cholinergic activation of M3 receptors on bronchial smooth muscle leads to an increase in intracellular Ca++ levels (via activation of the g-coupled receptor Gq), resulting in contraction of airway smooth muscle and bronchoconstriction[12]. Muscarinic receptor antagonists block the parasympathetic cholinergic induced bronchoconstriction and may reduce mucus hypersecretion[12]. The effectiveness of inhaled antimuscarinic agents in the long-term management of asthma has not been fully demonstrated, and therefore muscarinic antagonist are not considered a first-line therapy for asthma[15]. However, cholinergic antagonists such as ipratropium, tiotropium, aclidinium, umeclidinium, and glycopyrrolate may assist asthma patients with more moderate to severe asthma, and may have additive benefit when used with an inhaled beta 2-agonists in patients with severe asthma exacerbations (e.g. Combivent)[16]. The inhaled muscarinic antagonists used for asthma and COPD are quaternary amines with low systemic absorption, reducing the potential for anti-muscarinic side effects. Muscarinic antagonists are divided into short-acting agents (ipratropium) and longer acting agents, such as tiotropium (Spiriva) and aclidinium bromide (Tudorza Pressair). Aclidinium has the unique property of being rapidly hydrolyzed in plasma resulting in low systemic exposure, thereby reducing potential side effects. The most common side effects of the muscarinic antagonists include dry mouth, pharyngitis, gastroenteritis, and headaches. As with any antimuscarinic drug, use with caution in patients with risk factors for prostatic symptoms (BPH), urinary retention, or closed angle glaucoma[10,11].

Leukotrienes (LT) have been shown to regulate the release of biochemical mediators from mast cells, eosinophils and basophils. These mediators have been shown to induce numerous biological effects, including increase in vascular permeability, increase in bronchiolar smooth muscle contraction, increase in mucus secretions, and augmentation of neutrophil and eosinophil migration. The actions of the leukotrienes are mediated by cysteinyl leukotriene receptors CysLT1 and CysLT2, which are present on mast cells, eosinophil, and endothelial cells. Zileuton (Zyflo) is a 5-lipoxygenase (enzyme) inhibitor, which has been shown to provide immediate & sustained improvement in Forced expiratory volume in one second (FEV1) (~15% vs placebo) in mild-to-moderate asthma, and moderate asthmatics had fewer exacerbations requiring oral steroids[17]. Zileuton has been shown to inhibit the metabolism of theophylline and warfarin, and therefore must be monitored. Zafirlukast (Accolate) and Montelukast (Singulair) are leukotriene receptor antagonists, which inhibit the CysLT1 leukotriene receptor, attenuating the late stage response to inhaled allergen and post-allergen induced bronchospasms. These agents have been shown to provide a modest improvement in FEV1 (~11% vs placebo), improve asthma symptoms, and reduce overall albuterol use. Both agents have been shown to increase warfarin half-life and must be monitored. While these drugs are generally well tolerated, zileuton has been associated with liver toxicity and occasional monitoring of liver function is recommended[11]. In addition, an increased risk of serious neuropsychiatric events, including suicide and suicide attempts has been reported with the use of montelukast[18]. All of these agents are oral therapies and can provide alternative therapy for mild-persistent asthma, alternative combination therapy with ICS for moderate persistent asthma, and an add-on therapy with ICS to avoid increasing doses of inhaled steroids[19]. While these agents have been shown to improve asthma symptom free-days, they tend to be less effective than ICS or long-acting beta-2 agonists as add-on therapy[20].

Omalizumab (Xolair), is a humanized monoclonal antibody given subcutaneously (SQ) that binds to and inhibits Immunoglobulin E (IgE), forming complexes with free IgE, thereby inhibiting

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IgE binding to mast cells and basophils, decreasing mediator release[21]. In patients with atopy, or excessive IgE concentrations in the blood that have difficulty controlling their asthma with standard therapies, omalizumab attenuates early and late phase airway responses to allergens and suppresses accumulation of eosinophils in the airways[22]. Omalizumab has been shown to improve quality of life, symptom control, and lung function, as well as reduce health care utilization. Omalizumab has been shown to be safe and well tolerated in adults and children[23].

Eosinophils are considered a key effector cell in the pathogenesis of allergic inflammation. Raised levels of eosinophils are present in 40–60% of asthmatics and are known to release mediators that promote airway inflammation in asthma. Increased levels of eosinophils in blood and the airways are highly correlated with symptom severity and frequency of exacerbations. Interleukin-5 (IL-5) is the principal eosinophilic regulatory cytokine, which regulates proliferation, maturation, differentiation, migration, and effector functions of eosinophils. Recently several new biologic agents have been approved to reduce the effects of eosinophilic asthma24. Mepolizumab (Nucala) and reslizumab (Cinqair) are used in severe prednisone-dependent eosinophilic asthma, and act by directly targeting IL-5[25]. Both drugs have been shown to significantly reduce exacerbations by >50%, Improve lung function, and reduce eosinophil numbers. Mepolizumab (Nucala) showed a 50% reduction in oral steroid dose[26,27]. Benralizumab (Fasenra) depletes eosinophils by binding with high specificity to interleukin-5 receptor-α on eosinophils and basophils. This results in increased antibody-dependent cell-mediated cytotoxicity and death of eosinophils and basophils via apoptosis. Benralizumab (Fasenra) reduced frequency of asthma exacerbations and oral glucocorticoid doses. Lastly, dupilumab (Dupixent) is an interleukin-4 receptor (IL-4Rα) antibody targeting the T helper cell (Th2) pathway to block differentiation and survival of Th2 cells. Dupilumab is a fully human monoclonal antibody that targets the IL-4Rα receptors for IL-4 and IL-13.

When Dupilumab targets the IL-4Rα, it reduces asthma symptoms by blocking the activation and recruitment of eosinophils, and Th2 and B cells[28]. These agents have been shown to be generally safe and well tolerated, with the most common adverse drug reactions (ADRs) include injection-site reactions, nasopharyngitis and upper respiratory tract infections, and headache.

Theophylline, once a commonly used medication for asthma patients, is a competitive, nonselective phosphodiesterase inhibitor, which leads to an increase in Cyclic adenosine monophosphate (cAMP) accumulation and bronchodilation. theophylline relaxes airway smooth muscle by inhibition of phosphodiesterase-3 (PDE3), although the degree of inhibition is relatively small at therapeutic concentrations. Theophylline also has an inhibitory effect on mediator release from alveolar macrophages, which is mediated primarily by inhibition of PDE4 activity. Theophylline is also an adenosine antagonist in bronchial smooth muscle. In asthma, adenosine induces bronchoconstriction and increased histamine release, an effect not seen in non-asthmatic patients. Theophylline provides mild to moderate bronchodilation and anti-inflammatory actions, but most studies show little or no effect on airway hyperresponsiveness. While sustained release formulations may be used as alternative asthma controller, it is not preferred to long-acting beta2 agonists, and is not recommended as 1st-line therapy for asthmatic patients. Doses must be titrated slowly because of the narrow therapeutic range and the potential for severe side effects. As a result, serum levels are monitored during chronic use to avoid toxicity. Adverse reactions and toxicity are relatively uncommon at serum theophylline levels <15 mcg/mL; however, at serum levels > 20 mcg/mL, about 75% of patients may have N/V, diarrhea, headache, insomnia, irritability and CNS effects (headache, anxiety, tremor), and at serum levels >35 mcg/mL, patients may experience hyperglycemia, hypotension, cardiac arrhythmias, tachycardia, seizures, brain damage, and even death[10,11].
Corticosteroids should be used for all persistent categories of asthma (ICS) and are the most potent and effective anti-inflammatory medication currently available. Long-acting beta2-agonists are used concomitantly with anti-inflammatory medications for symptom control. Leukotriene inhibitors provide alternate therapy to low dose ICS in mild asthma or add-on therapy in more persistent asthma. Antimuscarinics may provide added benefit to inhaled beta2-agonists in severe exacerbations. Combination therapies such as Advair Diskus (fluticasone + salmeterol), Symbicort (budesonide + formoterol), Dulera (mometasone + formoterol), and Breo Ellipta (Fluticasone and vilanterol) provide a convenience for the asthmatic patient and can help with compliance.

In lieu of the recent COVID-19 pandemic, GINA provides the following guidance:
Because COVID-19 causes breathing difficulties, asthmatic patients are at a higher risk for developing more severe and life threatening symptoms if infected[1]. Patients should be advised to continue taking inhaled corticosteroid (ICS) containing medications as well as any add-on therapies, if prescribed. The stoppage of ICS is associated with worsening of asthmatic symptoms. Ensure that the patient maintains a written asthma action plan to help recognize situations, which call for emergency treatment[1].

For healthcare professionals, GINA recommends the avoidance of nebulizer solutions, when possible. Respiratory particles may be transmitted to a distance of 1 meter, increasing the risk of infection to others in the facility. An alternative to nebulizers is a pressurized meter-dose inhaler with a spacer. Furthermore, GINA recommends that for patients with confirmed or suspected COVID-19, spirometry tests be postponed unless there is an urgent need[1].

The new GINA report, released in March of 2020, provide the following updates to the 2019 report

- SABA only treatment for adults or adolescents is still no longer recommended as the preferred reliever[1]. **See Figure 1.**
- The use of as-needed ICS-formoterol in mild asthma is reinforced, to help

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prevent over reliance on SABAs[1,29]. Of note, GINA only refers to the ICS-formoterol combination for this purpose, yet this medication has not been approved in the U.S. as reliever therapy[1]. **See Figure 1.**

- Phenotyping is unnecessary for prescribing as-needed ICS-formoterol in patients with mild asthma[1].
- For mild asthma, the maximum daily dose of formoterol is 48mcg when using beclomethasone-formoterol and 72mcg formoterol when using budesonide-formoterol, and such doses have been rarely found in clinical trials[1].
- For African-American children aged 6-17 years, there is additional evidence to support the use of an ICS whenever a short-acting beta agonist (SABA) is taken[1].
- The ICS dosing table has been revised to 'low,' 'medium,' and 'high' doses to better correlate with doses commonly used in clinical practice.

See Tables 1 and 2[1].

- For preschoolers with asthma, daily ICS shows superior efficacy to leukotriene receptor antagonists (LTRAs) for controlling symptoms and preventing exacerbations. Furthermore, alerts have been added to montelukast pertaining to an increased risk of serious mental health effects in all age groups[1].

High dose ICS is no longer recommended at Step 4 of children aged 6-11 years[1]. **See Figure 3.**

It is important to note the differences between the GINA 2020 recommendations and the NHLBI EPR-3 guidelines. Though there are similarities, there numerous differences as well.

GINA 2020 vs. EPR-3:

The GINA 2020 recommendations and the EPR-3 2018 guidelines are structured similarly. **See Figures 1-6.** Both publications separate their respective findings into three age groups and utilize stepwise treatment approaches and assessments of severity based on patient

Figure 1:

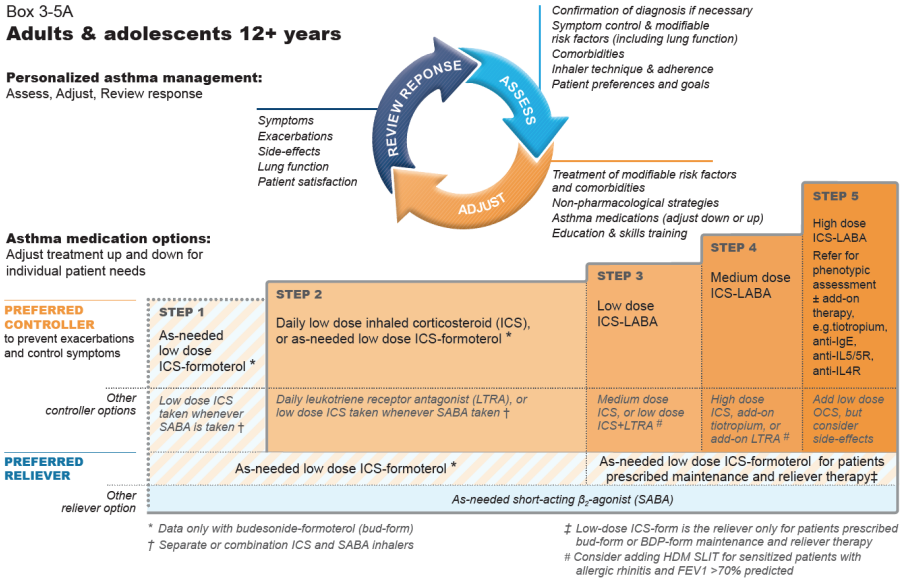
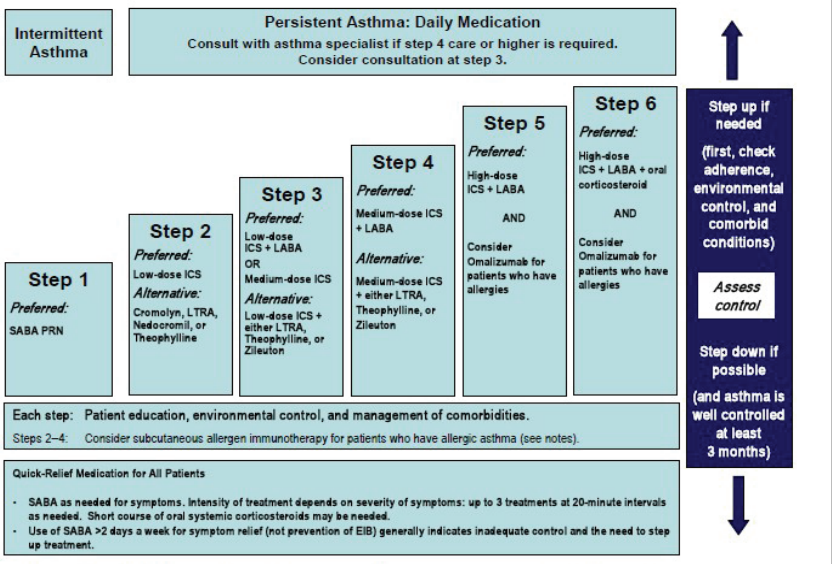


Figure 2:

FIGURE 4–5. STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥12 YEARS OF AGE AND ADULTS



— Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, long-acting inhaled beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral systemic corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.
- Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LTRA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B, and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D for zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on (EPR—2 1997) and Evidence B for omalizumab.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.
- Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.

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WHAT'S NEW IN THE TREATMENT OF ASTHMA?
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interview. However, there are notable differences, discussed below: For all patients five years and greater, EPR-3 categories asthma severity into four categories: intermittent, mild, moderate, and severe. For children ages six years and greater, GINA categorizes asthma into three categories: well controlled, partly controlled, and uncontrolled. However, for children ages 0-4 years, EPR-3 classifies asthma control as well controlled, not well controlled, and very poorly controlled. Both publications evaluate the frequency of patient symptoms, nighttime awakenings, SABA usage, and interference with normal activity, but EPR-3 also incorporates lung function tests (except for children ages 0-4 years), whereas, GINA does not[1,4].

The GINA recommendations only describe five steps in the stepwise treatment of asthma whereas EPR-3 describes six.

For all patients 12 years and greater, GINA recommends ICS-formoterol as a preferred reliever agent, with a SABA listed as a "reliever option." **See Figure 1**. EPR-3 recommends a SABA at all stages of asthma for all patients[1,4]. **See Figures 2,4, and 6.**

There are several other differences between the two publications with regards to the placement of specific therapeutic agents. For example, the cromolyn appears in Step 2 of EPR-3, but does not appear anywhere in the GINA approach. The differences regarding the medications are too numerous to discuss with text, and so, are provided below.

The Role of the Pharmacist:

Patient education is critical for proper asthma management. The pharmacist should communicate to the patient the difference between maintenance and rescue medications and also verify that the patient uses proper technique when administering the medication. If the medication includes a dose counter, the pharmacist should instruct the patient to seek a refill before the inhaler is empty[30].

For children initiating inhaler therapy, a pharmacist should recommend the use of a spacer until proper technique is

Table 1:

Adults and adolescents (12 years and older)			
Medication	**Daily dose (mcg)**		
	Low	Medium	High
Beclometasone dipropionate (HFA)	100–200	>200–400	>400
Budesonide (DPI)	200–400	>400–800	>800
Ciclesonide (HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100	n.a.	200
Fluticasone propionate(DPI)	100–250	>250–500	>500
Fluticasone propionate (HFA)	100–250	>250–500	>500
Mometasone furoate	110–220	>220–440	>440
Triamcinolone acetonide	400–1000	>1000–2000	>2000
Children (6-11 years)			
Beclometasone dipropionate (HFA)	50-100	>100-200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide	80	>80-160	>160
Fluticasone furoate (DPI)	n.a.	n.a.	n.a.
Fluticasone propionate (DPI)	100–200	>200–400	>400
Fluticasone propionate (HFA)	100–200	>200–500	>500
Mometasone furoate	110	≥220–<440	≥440
Triamcinolone acetonide	400–800	>800–1200	>1200

Table 2:

Children (0-5 years)	
Medication	**Low Total Daily Dose**
(mcg)	
Beclometasone dipropionate (HFA)	50 (ages 5 and older)
Budesonide (DPI)	500 (ages 1 and older)
Ciclesonide (HFA)	Not sufficiently studied in this age group
Fluticasone propionate	50 (ages 4 and older)
Fluticasone furuoate	Not sufficiently studied in this age group
Mometasone furoate	100 (ages 5 and older)

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observed. If a spacer is used, the pharmacist should verify that the patient first shakes the medication for five seconds, exhales completely, places lips tightly around the mouthpiece, pushes the actuator as they begin to inhale, then holds breath for five seconds. If there is no spacer used, the patient may seal the lips around the mouthpiece or one to two inches away and follow the same steps. If the patient uses a nebulizer, ensure the patient can load the device correctly and place the mask around the nose and mouth. With all devices, emphasize the importance of cleaning when appropriate[3]. For example, the QVAr Redihaler should be cleaned once weekly with a dry cloth or tissue, but never washed with water[31].

The pharmacist should also stress the importance of maintenance medication compliance and educate the patient that over reliance on reliever medications could lead to remodeling in the airways and poor outcomes later[1].

Finally, the pharmacist should see that the patient has a customized written asthma action plan in order to avoid triggers, manage symptoms, and seek emergency care if needed.[2] A written asthma action plan helps the patient understand the appropriate response whenever symptoms occur, especially in regard to worsening asthma. A "green" zone indicates that the patient is without symptoms and is not restricted in usual activities. With the "green" zone, there are also places to record peak flow as well as what medications were taken, their respective doses, and when to take them. A "yellow" zone is indicative of coughing, wheezing, shortness of breath and a mild restriction of usual activities. In this phase, there should be a description for taking reliever medications and what to do if symptoms and peak flow do not improve. A "red" zone depicts severe symptoms and the potential for emergency care. In this phase, the patient is very short of breath, persistent or worsening symptoms over the past 24 hours, an inability to perform usual activities, and an ineffective to reliever medications1. Provided below is sample action plan for the EPR-3[33]: **See Figure 7.**

Figure 3:

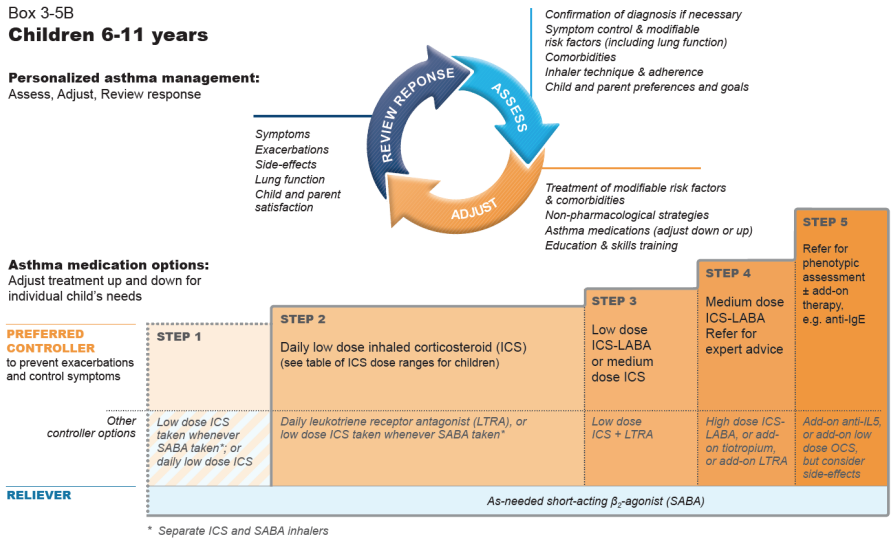
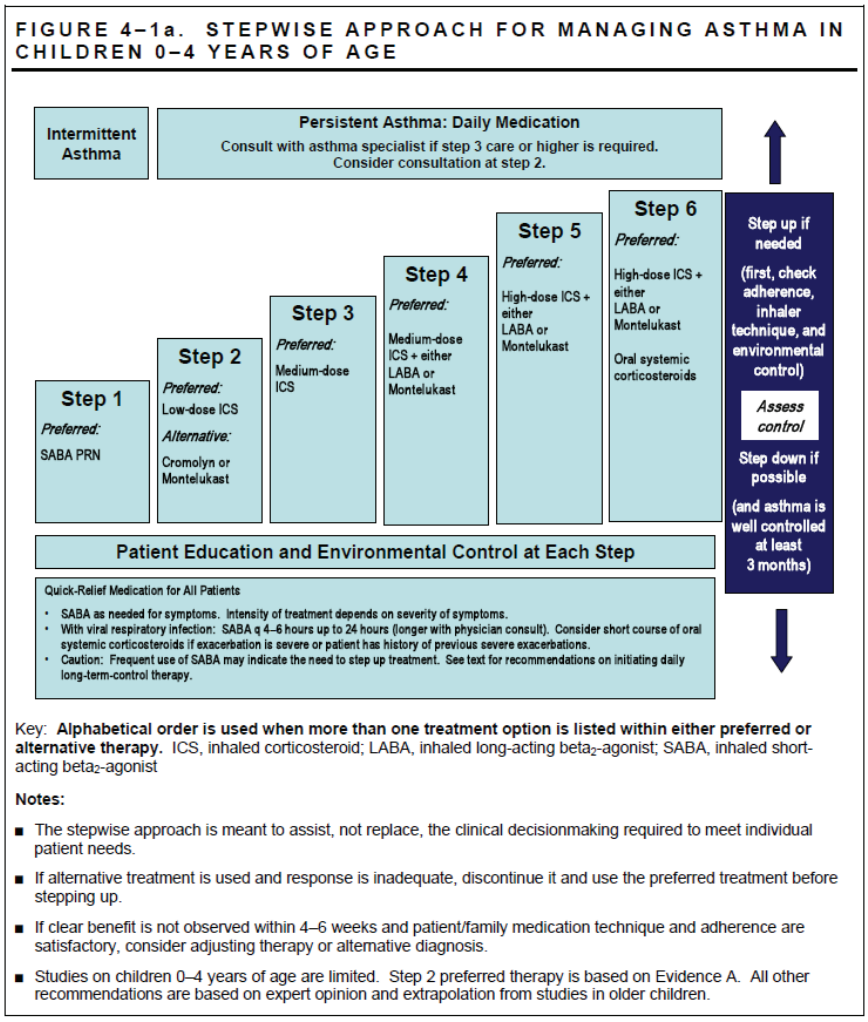


Figure 4:



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WHAT'S NEW IN THE TREATMENT OF ASTHMA?
AN UPDATE TO THE GUIDELINES

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Figure 5:

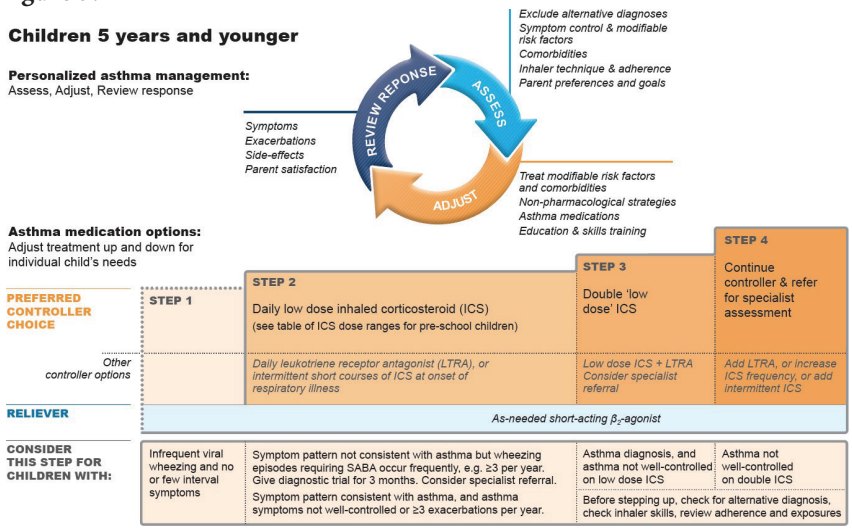
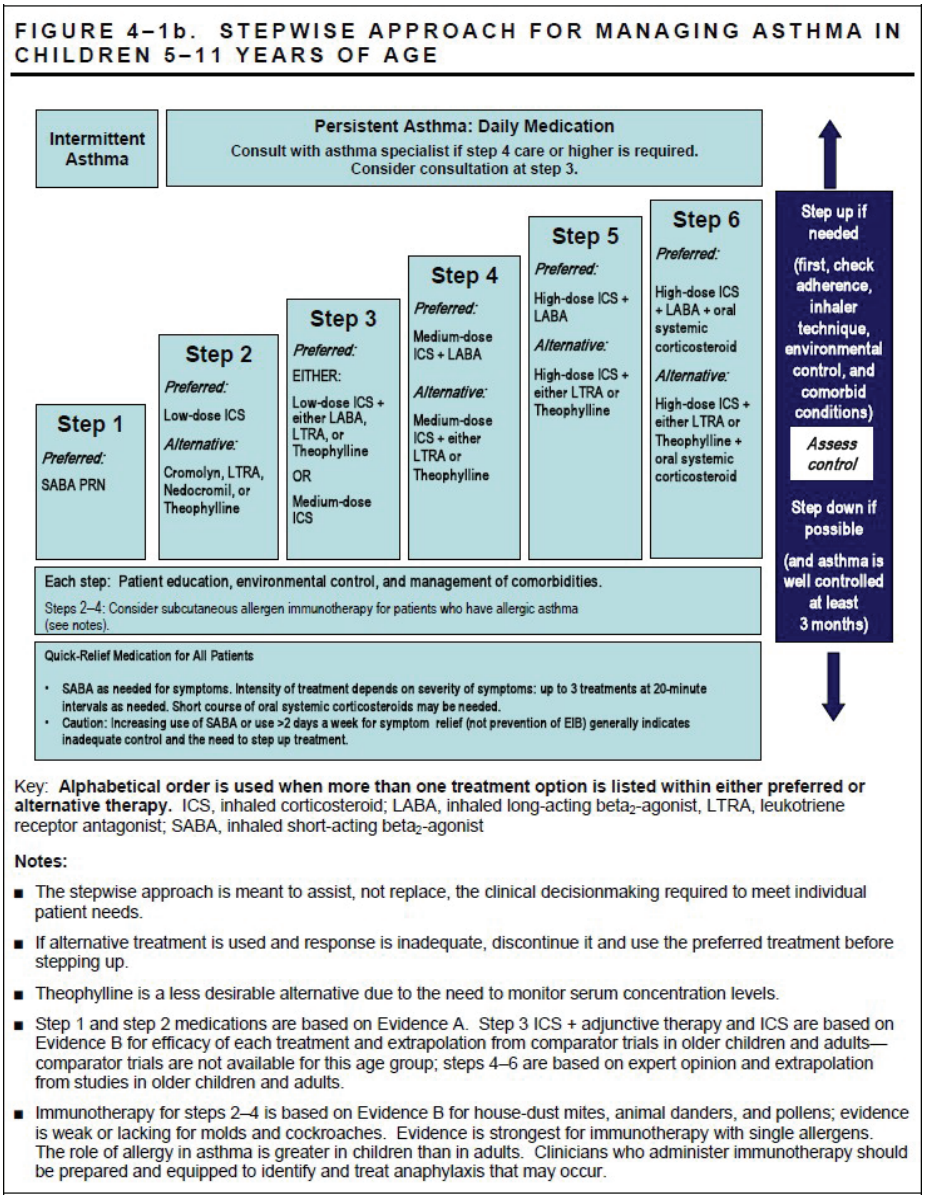


Figure 6:



Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** ICS, inhaled corticosteroid; LABA, inhaled long-acting beta$_2$-agonist, LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

Notes:

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Theophylline is a less desirable alternative due to the need to monitor serum concentration levels.
- Step 1 and step 2 medications are based on Evidence A. Step 3 ICS + adjunctive therapy and ICS are based on Evidence B for efficacy of each treatment and extrapolation from comparator trials in older children and adults—comparator trials are not available for this age group; steps 4–6 are based on expert opinion and extrapolation from studies in older children and adults.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults. Clinicians who administer immunotherapy should be prepared and equipped to identify and treat anaphylaxis that may occur.

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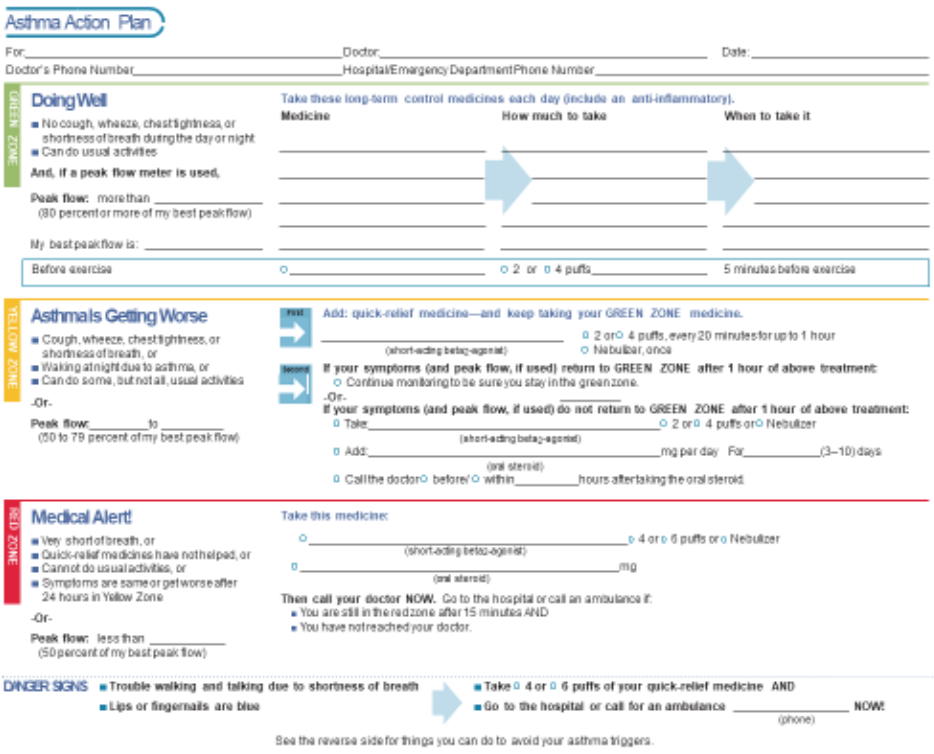
Figure 7:



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WHAT'S NEW IN THE TREATMENT OF ASTHMA? AN UPDATE TO THE GUIDELINES

INSTRUCTIONS: After completing the quiz below complete the information to the left and mail to MPhA, PO Box 16861, Jackson, MS 39236 including a self-addressed stamped envelope OR scan and email to CE@mspharm.org. A minimum grade of 70% is required to earn credit for this CE. This is a free service for MPhA Members.

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1. A 9-year-old child is prescribed daily beclomethasone in addition to albuterol as a reliever. After a recent visit to a pulmonologist, it is determined that the child's symptoms are poorly controlled. From the recommendations, which of the following medications would be the PREFERRED agent at this step? Select one.
   a. Low dose ICS-LABA.
   b. Low dose ICS plus a LTRA.
   c. Medium dose ICS-LABA plus tiotropium.
   d. Low dose ICS-LABA plus prednisone.

2. A 30-year-old asthmatic patient is currently taking low dose budesonide plus montelukast. After a recent visit to her pulmonologist, she is regarded as having poor control over her symptoms. (Assume the patient has an as needed SABA as a reliever in all options below.) According to the guidelines, which is the PREFERRED option for this patient? Select one.
   a. Advair 250mcg/50mcg.
   b. High dose budesonide plus tiotropium.
   c. High dose budesonide plus montelukast.
   d. As needed formoterol.

3. Approximately, what percentage of children ages 0-17 years has asthma?
   a. 50%
   b. 25%
   c. 10%
   d. 5%

4. Which medication is associated with a risk of serious adverse mental health effects?
   a. Montelukast
   b. Ipratropium
   c. Omalizumab
   d. Advair

5. Patient counseling for asthmatics should include:
   a. The importance of a written asthma action plan.
   b. The importance of timely refilling of needed prescriptions.
   c. An inspection and verification of proper inhaler technique.
   d. All of the above

6. Which ICS-LABA product has been studied for relief from asthmatic symptoms?
   a. Advair
   b. Dulera
   c. Breo
   d. Symbicort

7. How often should the QVAR Redihaler be cleaned?
   a. Daily
   b. Weekly with a tissue or dry cloth
   c. Weekly with warm soap and water
   d. Never

8. Which of the following statements is TRUE of the NHLBI EPR-3 Guidelines?
   a. EPR-3 lists five steps for adults and adolescents greater than 12 years.
   b. EPR-3 does NOT list symbicort as reliever therapy.
   c. EPR-3 recommends referral for phenotypic assessment at later stages of therapy.
   d. EPR-3 does NOT incorporate lung function tests in patient therapy assessment.

9. Which of the following statements is TRUE concerning Step 4 of the GINA 2020 recommendations for children 6 to 11 years?
   a. High dose ICS is no longer recommended.
   b. ICS-formoterol is a preferred reliever.
   c. Theophylline is listed as an adjunctive controller option.
   d. Magnesium nebulizers are listed as a reliever option.

10. At what steps of the GINA 2020 recommendations are LTRAs recommended as controller options? Select all that apply.
    a. Step 1
    b. Step 2
    c. Step 3
    d. Step 4

11. Which of the following is a humanized monoclonal antibody that is given subcutaneously, that binds to IgE, thereby inhibiting IgE binding to mast cells and basophils, and decreasing mediator release in asthmatic patients?
    a. Ipratropium (Atrovent)
    b. Zileuton (Zyflo)
    c. Omalizumab (Xolair)
    d. Zafirlukast (Accolate)

12. Which of the following drugs will block bron choconstriction elicited by increased parasympathetic tone?
    a. Fluticasone
    b. Tiotropium
    c. Serevent
    d. Albuterol

13 A 9-year-old boy has asthma, which has required four hospitalizations in the last year. His only medication was an albuterol inhaler. Since his last hospital stay, he started receiving daily maintenance therapy of a drug that inhibits the inflammatory response and immunogenic mediators associated with asthma. This drug has greatly reduced the frequency of these severe attacks. Which of the following therapies is most likely responsible for this benefit?
    a. Albuterol (Ventolin) administered via nebulizer
    b. Theophylline administered orally
    c. Fluticasone (Flovent HFA) administered via inhaler
    d. Zafirlukast (Accolate) administered orally

14. Patients using an inhaled corticosteroid (ICS) are counseled to wash their mouth following is use dueto an increased likelihood of:
    a. Nasal stuffiness
    b. Candidiasis (Oral thrush)
    c. Cushing's Syndrome
    d. Addisonian crisis

15. What is the most appropriate place in therapy for long-acting beta-agonists such as salmeterol in asthmatic patients?
    a. As monotherapy
    b. As rescue therapy
    c. In combination with inhaled corticosteroids
    d. Long-acting beta-agonists are only used for COPD

16. Which of the following biologic monoclonal agents binds with high specificity to the interleukin-5 receptor-α on eosinophils and basophils?
    a. Benralizumab
    b. Mepolizumab
    c. Reslizumab
    d. Omalizumab

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