PHARMACIST CE:
An Overview of Recommended Asthma Treatments with New and Emerging Medications for Use

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Asthma is a unique disease state that has the ability to plague an individual starting early in childhood and persisting throughout their adult life. Characterized by chronic airway inflammation associated with reversible airflow obstruction and airway hyperresponsiveness, asthma results from the interplay between genetic and environmental factors.1

Approximately 9.5% and 8.2% of US children and adults, respectively, have a diagnosis of asthma.2 It accounts for over $50 million US in health care costs per year and results in 14.2 million office and 1.8 million emergency department visits per year.2

Clinical Presentation

Asthma causes symptoms such as cough, shortness of breath (SOB), wheezing, and chest tightness, that are often relapsing and remitting in nature. Direct causes of these symptoms include airway narrowing, airway wall thickening, and increased mucus production. Typically, asthma is diagnosed based on two key factors: history of respiratory symptoms (e.g. cough, SOB, wheezing, chest tightness) and reversible airflow limitation (based on spirometry). Reversible airflow limitation is defined by a 1-second forced expiratory volume (FEV1) increase of more than 12% and 200mL after administration of a short-acting beta-agonist (SABA). Risk factors for developing asthma can be found in Table 1.3

To date, no interventions have shown a causal relationship in reducing the risk of developing asthma. However, one Danish cohort study suggests that fish oil supplementation in the third trimester of pregnancy is associated with a reduced incidence of recurrent wheeze in the newborn infant.4

Assessment and Management

Assessment of asthma is divided into two domains, symptom control and future risk of adverse outcomes (e.g. exacerbations, airflow limitations, and medication side effects).3 Other guidelines, such as the Guidelines for the Diagnosis and Management of Asthma (EPR-3) by the National Heart, Lung and Blood Institute have produced assessment tools useful for classifying severity and level of asthma control for both children and adults.5 These charts are particularly useful for the initial classification of asthma severity in addition to assessing level of control. For the purposes of this review, the 2018 Global Strategy for Asthma Management and Prevention from the Global Initiative for Asthma (GINA 2018) will be the primary focus. According to GINA 2018, initial asthma severity can be classified as mild, moderate, or severe. Assessing the level of control for follow-up visits can be classified as well-controlled, partially-controlled, or uncontrolled.5 While evaluating literature regarding the management of asthma it is important to note that there is variance in organizational recommendations about the assessment and classification of asthma. Depending on the study, there may be slight variance among asthma severity and phenotype depending upon how the study was conducted and which guidelines were referenced.

### TABLE 1. Risk Factors for Developing Asthma

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Parent with asthma</td>
</tr>
<tr>
<td>Parent smoking before child 1 year of age</td>
</tr>
<tr>
<td>Eczema at 4 years of age</td>
</tr>
<tr>
<td>Atopy at 4 years of age</td>
</tr>
<tr>
<td>Recurrent chest infections at 2 years of age</td>
</tr>
<tr>
<td>Antibiotic use before child 1 year of age</td>
</tr>
</tbody>
</table>

ACRONYM KEY

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-IgE</td>
<td>anti-immunoglobulin E</td>
</tr>
<tr>
<td>Anti-IL5</td>
<td>anti-Interleukin-5</td>
</tr>
<tr>
<td>CFC</td>
<td>chlorofluorocarbon</td>
</tr>
<tr>
<td>DPI</td>
<td>dry-powder inhaler</td>
</tr>
<tr>
<td>EPR-3</td>
<td>Expert Panel Report – Guidelines for the Diagnosis and Management of Asthma</td>
</tr>
<tr>
<td>FEV1</td>
<td>1-second forced expiratory volume</td>
</tr>
<tr>
<td>GINA</td>
<td>Global Initiative for Asthma</td>
</tr>
<tr>
<td>HFA</td>
<td>hydrofluoroalkane</td>
</tr>
<tr>
<td>ICS</td>
<td>inhaled corticosteroid</td>
</tr>
<tr>
<td>LABA</td>
<td>long-acting beta-agonist</td>
</tr>
<tr>
<td>LAMA</td>
<td>long-acting muscarinic antagonist</td>
</tr>
<tr>
<td>LM</td>
<td>leukotriene modifier</td>
</tr>
<tr>
<td>LTRA</td>
<td>leukotriene receptor antagonist</td>
</tr>
<tr>
<td>MDI</td>
<td>metered-dose inhaler</td>
</tr>
<tr>
<td>OCS</td>
<td>oral corticosteroid</td>
</tr>
<tr>
<td>OTC</td>
<td>over-the-counter</td>
</tr>
<tr>
<td>PRN</td>
<td>as needed</td>
</tr>
<tr>
<td>SABA</td>
<td>short-acting beta-agonist</td>
</tr>
<tr>
<td>SiT</td>
<td>single inhaler therapy</td>
</tr>
<tr>
<td>SOB</td>
<td>shortness of breath</td>
</tr>
<tr>
<td>TSLP</td>
<td>Thymic stromal lymphopoietin</td>
</tr>
</tbody>
</table>


NOT FOR REPRODUCTION
According to GINA 2018, assessing level of symptom control relies on the following parameters:

- Daytime symptoms more than twice per week
- Any nighttime awakening due to asthma
- Use of reliever inhaler more than twice per week
- Limitation in activities due to asthma.

Patients are well-controlled if they do not meet any of the criteria, are partly controlled if they possess 1-2 of the criteria and are uncontrolled if they possess 3 or all of the criteria.5

There are numerous, modifiable risk factors to consider even in patients who otherwise have few asthma symptoms. They are summarized in Table 2.5

**Therapeutic Approach to Asthma Control and Risk Reduction**

A stepwise approach should be used after assessment of a patient’s asthma control. The stepwise approach consists of increasing or decreasing the dose and/or number of medications and frequency of administration as level of control worsens or improves. Several strategies exist for stepping up or stepping down therapy, however, guidelines agree that periodic medication adjustments that are most beneficial for the patient and provider are warranted. For example, according to GINA 2018 it is acceptable to either increase the dose of an ICS or maintain the current dose of an ICS and add a long-acting beta-agonist (LABA) for patients with uncontrolled asthma. Table 3 provides a summary of the treatment considerations for each step of therapy.

**Available Asthma Reliever Medications**

**Short-Acting Beta Agonists (SABA)** - A staple of asthma therapy consists of reliever medications intended to relieve asthma symptoms acutely. Commonly available SABA options include albuterol (ProAir®, Proventil®, Ventolin®) and levalbuterol (Xopenex®). SABAs work by relaxing bronchial smooth muscle tissue leading to bronchodilation. Table 4 summarizes key points when considering SABA use.

**TABLE 2. Risk Factors for Poor Asthma Control**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
</table>
| ICS not prescribed | Patients were more likely to have exacerbations.
| Poor adherence | Higher risk of exacerbations.
| Incorrect technique | Increased risk of exacerbations.
| High SABA use | Increased risk of exacerbations.
| Low FEV1 | Especially <60% predicted.
| Higher bronchodilator reversibility | Risk increases.
| Major psychological or socioeconomic problems | Increased risk of exacerbations.
| Smoking or allergen exposure | Increased risk of exacerbations.
| Presence of obesity | Increased risk of exacerbations.
| Chronic sinusitis | Increased risk of exacerbations.
| Confirmed food allergy | Increased risk of exacerbations.
| Sputum or blood eosinophilia | Increased risk of exacerbations.
| Pregnancy | Increased risk of exacerbations.

**TABLE 3. Stepwise Approach to Asthma Treatment**

<table>
<thead>
<tr>
<th>Severity Classification</th>
<th>STEP in Therapy</th>
<th>Preferred Controller Medication</th>
<th>Alternative Controller Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>STEP 1</td>
<td>N/A</td>
<td>Low-dose ICS</td>
</tr>
<tr>
<td></td>
<td>STEP 2</td>
<td>Low-dose ICS</td>
<td>LTRA</td>
</tr>
<tr>
<td>Moderate</td>
<td>STEP 3</td>
<td>Low-dose ICS + LABA</td>
<td>Medium/high-dose ICS OR Low-dose ICS + LTRA</td>
</tr>
<tr>
<td>Severe</td>
<td>STEP 4</td>
<td>Medium/high-dose ICS + LABA or theophylline</td>
<td>Add tiotropium OR Medium/high-dose ICS + LTRA or theophylline</td>
</tr>
<tr>
<td></td>
<td>STEP 5</td>
<td>Specialist referral for add-on controller treatment methods*</td>
<td>Add low-dose OCS</td>
</tr>
</tbody>
</table>

ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid

*Tiotropium, anti-immunoglobulin E (anti-IgE), or anti-Interleukin-5 (anti-IL5) treatment options recommended based on patient characteristics and provider recommendation

**ProAir Respliclick** is a novel device that eliminates the need for actuation by using dry powder as opposed to a propellant.7 For this reason, the ProAir Respliclick® can’t be used with a spacer. This is a key difference that should be communicated with patients when they are transitioned from the ProAir HFA® inhaler to the ProAir Respliclick® inhaler.

SABAs can cause tremors, shakiness, palpitations, hypokalemia, tachycardia, and hyperglycemia. Patients should be educated to monitor for symptom frequency, days of SABA use, and use of peak flow. A peak flow meter is a handheld device that measures how well air moves out of a patient’s lungs. During periods of worsening asthma, airways narrow and the patient’s peak flow reading decreases. Clinicians can consider monitoring blood pressure, heart rate, plasma glucose, and serum potassium.

Most MDIs should be shaken and primed before first use and generally must...
be re-primed after 7-14 days of no use, depending on the specific inhaler.\(^8\)

Low-Dose ICS + Formoterol - For patients with moderate-to-severe asthma, or who are not well controlled on inhaled corticosteroid (ICS) monotherapy, a combination of low-dose budesonide + formoterol (Symbicort\(^\text{®}\)) can be used as both a reliever therapy and maintenance therapy, referred to as single-inhaler therapy (SIT). For example, patients could be prescribed Symbicort\(^\text{®}\) to be used twice daily as a maintenance inhaler, with instructions to also use PRN as a reliever therapy. According to a systematic review published in 2013 by Cates and Karner, SIT with budesonide and formoterol can reduce the risk of asthma exacerbations requiring the need for oral corticosteroids. However, the studies included adults >18 years of age, thus precluding the use of single-inhaler therapy in children. There were higher rates of discontinuation among uses of single-inhaler therapy and has little impact on rates of hospitalization.\(^9\) More information regarding the Symbicort\(^\text{®}\) inhaler can be found in the controller therapy section.

### Available Asthma Controller Medications

#### Inhaled Corticosteroid (ICS)

**Monotherapy** - ICS inhalers are available as monotherapy or combination therapy, as well as dry-powder inhaler (DPI) or metered-dose inhaler (MDI) options. ICS therapy is considered the cornerstone of controller therapy for patients with asthma that is not well controlled and should be considered first-line. ICS therapy inhibits the inflammatory response of bronchial tissues and improves airflow.\(^1\)

ICS therapy can cause dysphonia, oral candidiasis, hoarseness, and cough. High-dose ICS use has also been associated with an increased risk of pneumonia and growth suppression in children. Patients should be educated to rinse their mouth after using an inhaler with an ICS to reduce the risk for developing oral candidiasis, monitor for symptom frequency, days of SABA use and use of peak flow. Clinicians can consider monitoring for signs of oral candidiasis and suppressed growth in children taking high doses of ICS products.\(^1\)

When referring to the stepwise approach for medication therapy, one must consider the ICS dose in terms of low, medium or high dose. Table 5 lists the dosing classification for commonly used ICS medications.\(^10\) The list is not all inclusive and only contains information on the ICS component if available in a combination inhaler.

Monotherapy ICS options are depicted

### TABLE 4. Available SABA Medications

<table>
<thead>
<tr>
<th>Brand Name (available strengths)</th>
<th>Device</th>
<th>Typical Dosing</th>
<th>Dose Counter</th>
<th>Use with Spacer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ProAir Digihaler(^\text{®}) 117mcg</td>
<td>DPI</td>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>ProAir Respliclick(^\text{®}) 90mcg</td>
<td>DPI</td>
<td>180 mcg every 4-6 hours PRN</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Ventolin(^\text{®}) HFA 90mcg</td>
<td>MDI</td>
<td></td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Proventil(^\text{®}) HFA 90mcg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol sulfate HFA 90mcg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol Solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.63mg/3mL, 1.25mg/3mL, 2.5mg/3mL</td>
<td>Nebulizer</td>
<td>1.25-5mg every 4-8 hours PRN</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xopenex HFA(^\text{®}) 45 mcg</td>
<td>MDI</td>
<td>90 mcg every 4-6 hours PRN</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Levalbuterol HFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45 mcg</td>
<td>MDI</td>
<td></td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Levalbuterol Solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.31 mg/3 mL, 0.63 mg/3 mL, 1.25 mg/0.5 mL, 1.25 mg/3 mL</td>
<td>Nebulizer</td>
<td>0.31-1.25 mg every 4-6 hours PRN</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Information above can be found in more detail within each product’s package insert

HFA: hydrofluoroalkane; DPI: dry-powder inhaler; MDI: metered-dose inhaler; PRN: as needed

### TABLE 5. Select ICS Potencies

<table>
<thead>
<tr>
<th>Inhaled Corticosteroid</th>
<th>Age ≥12 Years</th>
<th>Age 5-11 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
<td>Medium</td>
</tr>
<tr>
<td>Beclomethasone (QVAR Redihaler(^\text{®}))</td>
<td>80-240 mcg</td>
<td>280-480 mcg</td>
</tr>
<tr>
<td>Budesonide (HFA)</td>
<td>320 mcg</td>
<td>320-640 mcg</td>
</tr>
<tr>
<td>Fluticasone furoate (Arnuity Ellipta(^\text{®}))</td>
<td>100 mcg</td>
<td>N/A</td>
</tr>
<tr>
<td>Fluticasone furoate (Breo Ellipta(^\text{®}))</td>
<td>100 mcg</td>
<td>N/A</td>
</tr>
<tr>
<td>Fluticasone propionate (Advair HFA)</td>
<td>176 mcg</td>
<td>264-440 mcg</td>
</tr>
<tr>
<td>Fluticasone propionate (Advair Diskus(^\text{®}))</td>
<td>200-300 mcg</td>
<td>350-500 mcg</td>
</tr>
<tr>
<td>Mometasone (Asmanex HFA)</td>
<td>220 mcg</td>
<td>330-440 mcg</td>
</tr>
</tbody>
</table>

in Table 6. Updates to inhaler devices include the addition of the Ellipta® inhaler. Arnuity Ellipta® is a once daily ICS that contains fluticasone. Comparatively, Flovent Diskus® is a twice daily ICS also containing fluticasone. The once daily administration of the Ellipta® device may improve patient compliance and ultimately the patient’s level of asthma control, although no head-to-head trials have been completed. Additionally, the Ellipta® device may have a simpler design which requires the patient to perform less steps to correctly use; however, this has not been evaluated in any studies.

The Redihaler® device is available as a replacement the HFA inhaler for QVAR®. The Redihaler® is an MDI which is slightly different than the traditional MDI. For this device, the patient does not actuate the device by pressing a button, rather it is the force of inspiration that activates the device to deliver a dose.11 Currently, QVAR® is the only available inhaler that utilizes the Redihaler® device.

**Inhaled-Corticosteroids (ICS) + Long-Acting Beta-Agonist (LABA) Combination Therapy** - For patients with moderate or severe asthma, consideration should be given to adding a LABA to the patient’s current therapy that already includes an ICS. Similar to ICS therapy, LABAs relax bronchial smooth muscle leading to bronchodilation. However, there is concern that chronic exposure to LABAs is associated with tolerance and reduced sensitivity to the bronchodilator effect. LABAs should therefore not be used as monotherapy for the maintenance treatment of asthma due to an increased risk of death, but still can be used in combination with an ICS.12 Available ICS/LABA combinations are summarized in Table 7.

As mentioned previously under monotherapy ICS devices, the Ellipta® device (such as Breo Ellipta®) is a once daily maintenance combination therapy option compared to the Advair® products which are all twice daily. One will notice the replacement of salmeterol/fluticasone propionate in Advair® with vilanterol/fluticasone furoate in Breo®. Studies have shown that this novel combination when used once daily can reduce the frequency of asthma exacerbations compared to placebo, but was not significantly different than traditional twice daily dosing of salmeterol/fluticasone.13

**Long-Acting Muscarinic Antagonist (LAMA) Therapy** - For patients with moderate-to-severe asthma, a LAMA can be used as a controller medication, often in addition to ICS/LABA combination controller therapy. For use in the treatment of asthma, tiotropium inhibits muscarinic receptors on smooth muscle causing bronchodilation. Although limited, there are high-quality studies assessing the effect of LAMAs on asthma control. One systematic review published in 2015 found that adding tiotropium to existing ICS therapy rather than increasing ICS dose may improve surrogate markers, such as lung function, but have not been shown to improve patient-oriented outcomes such as hospitalizations from asthma exacerbations, presentation to the emergency department, control of asthma or quality of life.14

Tiotropium is available as the Spiriva Respimat® soft mist inhaler device. It is important to note that the Spiriva Handihaler® device and capsules have not been approved for the treatment of asthma. Daily doses greater than 2.5 mcg have not been shown to confer additional benefit. Care should be given to prescribing and dispensing as the Spiriva Respimat® inhaler is available in concentrations of 1.25 mcg/actuation (asthma) and 2.5 mcg/actuation (COPD). The Respimat® inhaler utilizes a unique delivery system to deliver a soft, gentler mist rather than a forceful spray. Therefore, it is unable to be used with a spacer. However, this technology could improve the deposition of medication into the lungs, rather than the mouth and throat because of the reduced propellant velocity. The Respimat® device includes a dose counter and requires assembly as the medication canister is provided separate from the delivery device. Patients should be
educated on the proper assembly and use of the device.

Non-Inhaler Asthma Controller Medications

Leukotriene Modifiers (LMs) - There are also non-inhaled controller medications available for patients suffering from severe asthma. Leukotriene modifiers include medications that block the leukotriene receptors (LTRAs) and those which inhibit 5-lipoxygenase. Available LTRAs include the orally active medications zafirlukast and montelukast. A newer medication, zileuton, is available and targets the 5-lipoxygenase enzyme which is primarily responsible for the formation of leukotrienes. All of these medications are orally active and provide patients with severe asthma a specialized treatment option when other forms of therapy have been exhausted. Advantages of these medications include oral administration and few side effects for most patients. Although there is data to support use, guidelines still note that LTRAs/LMs are considered less effective than ICS medications. These medications may be useful in patients who struggle or are unwilling to use inhalers, have experienced side effects with ICS use, or have concomitant allergic rhinitis as an initial controller option in mild asthma. It may also be considered as add on therapy in moderate or severe asthma though the effectiveness is limited.13

Theophylline - Theophylline remains a recommended treatment option in some patients with moderate or severe asthma as add-on therapy to control symptoms and reduce risk of exacerbation. It is not recommended for the management of asthma in children or for those with mild symptoms. Theophylline is a therapy that has fallen out of favor in current guidelines for asthma treatment due to its limited efficacy, narrow therapeutic window for treatment, difficulty to manage, and possible toxicity related to use.3 For patients who require theophylline use in asthma control, it is best that they be managed closely by their provider. Current guidelines recommend exhaustion of most other possible alternatives before using in this condition for adolescents or adults.3,15

Newer Medications in the Management of Asthma

Although new therapies are constantly being discovered, the diagnosis and step-wise approach of treatment has been generally consistent from previous guidelines. Changes in therapy recommendations are mostly seen for those patients who present with “severe” (“treatment-resistant” or “refractory”) forms of asthma, or those with specific asthma diagnoses requiring specialist intervention. The emergence of breakthroughs in biologic therapies have given a new treatment option for patients with “treatment-resistant” or “refractory” asthma. Recently, there has also been a reintroduction of a previously available agent used for asthma relief over-the-counter. Some of the newly FDA-approved products can be noted in the following sections and Table 8. Although this list is not exhaustive, it highlights those products that officially carry an indication of asthma. With the discovery of these newer controller agents, providers may be able to minimize use of regular high-dose corticosteroids (oral or inhaled) and improve daily control of symptoms for patients while reducing risk for exacerbation. There are also several pipeline therapies and other non-drug methods which are emerging as popular treatments in certain asthma diagnoses. One example is sublingual immunotherapy for those suffering from asthma related to allergen exposure.5,16,17

<table>
<thead>
<tr>
<th>TABLE 7. Available Combination ICS/LABA Inhalers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand Name</strong> (available strengths)</td>
</tr>
<tr>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Salmeterol/fluticasone propionate</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td>Vilanterol/fluticasone furoate</td>
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<tr>
<td>Formoterol/budesonide</td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Formoterol/mometasone</td>
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</table>

*Information above can be found in more detail within each product’s package insert

Epinephrine Inhalation Aerosol (Primatene® Mist)

Primatene® Mist is now the only available OTC inhaler on the market. It acts as a bronchodilator to open the airways and is specifically indicated for the relief of mild symptoms associated with asthma.
with intermittent asthma in patients ≥12 years, and only for those who have been diagnosed with asthma by a health care provider. It is dosed as one inhalation (0.125 mcg/inhalation) of epinephrine as needed for symptom relief with at least 1 minute between repeat inhalations, and a maximum of 8 inhalations in 24 hours. The FDA recommends patients see a doctor if asthma is not better within 20 minutes of use, if symptoms get worse, if more than eight inhalations are needed in a 24-hour period, or if they experience more than two asthma attacks in a week.

Primatene® Mist was originally approved for OTC use by the FDA in 1967 as an treatment for asthma symptoms requiring immediate relief, who have been diagnosed with asthma, and are being managed by their healthcare provider. It may be advisable for pharmacies to keep Primatene® Mist behind the counter so that patients who purchase the product can be properly educated.

**Benralizumab (Fasenra™)**

Benralizumab is an anti-IL-5 monoclonal antibody medication that specifically targets IL-5 and blocks it from binding to receptor-α (IL-5R-α). This product was FDA approved in November 2017 as 30 mg subcutaneous injections every 4 weeks for 3 doses, then continued once every 8 weeks for add-on maintenance treatment of patients with severe asthma ≥12 years with an eosinophilic phenotype. Studies of benralizumab have demonstrated a decrease in asthma exacerbations in severe eosinophilic asthma.17,21 Previous guidelines have made note of other available anti-IL5 monoclonal antibody products such as mepolizumab (subcutaneous injection) and reslizumab (intravenous injection), with newer guidelines now including benralizumab as another add-on maintenance therapeutic option following successful trials in use for the treatment of asthma and prevention of exacerbations. Phase 2b trials saw significant reductions in the occurrence of asthma exacerbation of up to 57% compared to placebo in patients with an elevated baseline eosinophil count.22,23 Early studies of this medication class produced varying results in terms of efficacy in treatment, but current evidence shows they are effective in patients who have elevated eosinophil levels and severe asthma. Possible common side effects include pharyngitis and headaches and patients who are taking corticosteroids should not abruptly discontinue steroid therapy while taking this medication. Based on current recommendations and evidence, therapy with benralizumab (and other anti-IL-5 agents) is best reserved for add-on maintenance treatment in the setting of severe asthma, specifically targeting eosinophil-high patients.

**Dupilumab (Dupixent®)**

Dupilumab is an anti-IL4 and anti-IL13 monoclonal antibody medication that specifically binds to and blocks the IL-4R-α and IL-13R-α1 receptors. This medication was approved by the FDA in September 2018 for the treatment of patients with severe asthma and severe, eosinophilic asthma. Studies of dupilumab have demonstrated a decrease in asthma exacerbations in severe eosinophilic asthma.24,25 Early studies of this medication class produced varying results in terms of efficacy in treatment, but current evidence shows they are effective in patients who have elevated eosinophil levels and severe asthma. Possible common side effects include pharyngitis and headaches and patients who are taking corticosteroids should not abruptly discontinue steroid therapy while taking this medication. Based on current recommendations and evidence, therapy with dupilumab (and other anti-IL-4 agents) is best reserved for add-on maintenance treatment in the setting of severe asthma, specifically targeting eosinophil-high patients.

**Tezepelumab (AMG 157)**

Tezepelumab is a humanized monoclonal antibody medication that specifically targets interleukin-13 (IL-13). It was approved by the FDA in September 2018 for the treatment of patients with severe, eosinophilic asthma. Studies of tezepelumab have demonstrated a decrease in asthma exacerbations in severe eosinophilic asthma.26,27 Early studies of this medication class produced varying results in terms of efficacy in treatment, but current evidence shows they are effective in patients who have elevated eosinophil levels and severe asthma. Possible common side effects include pharyngitis and headaches and patients who are taking corticosteroids should not abruptly discontinue steroid therapy while taking this medication. Based on current recommendations and evidence, therapy with tezepelumab (and other anti-IL-4 agents) is best reserved for add-on maintenance treatment in the setting of severe asthma, specifically targeting eosinophil-high patients.
Three maintenance doses (70 mg every 4 weeks, 210 mg every 4 weeks, or 280 mg every 2 weeks) of this medication, all administered as subcutaneous injection, were evaluated, and demonstrated a reduction in clinically significant asthma exacerbations based on the calculated annualized asthma exacerbation rate (events per patient year) when added to long-acting beta-agonists and medium-to-high doses of inhaled glucocorticoids at all doses. When comparing the evaluated maintenance doses exacerbation rates were reduced in the low- (0.26), medium- (0.19), and high-dose (0.22) groups compared to placebo (0.67). This translated to a relative reduction of asthma exacerbations by 61%, 71%, and 66% for the respective doses. The most common adverse effects reported in the trial were asthma-related nasopharyngitis, headaches, and bronchitis. Currently this medication is undergoing Phase III trials but was granted breakthrough designation by the FDA in September 2018, opening the door for a new mechanism in the treatment of asthma. This medication will likely be best for a wider spectrum of patients suffering from severe asthma and who currently are uncontrolled with use of ICS/LABA maintenance therapy with or without oral corticosteroids, and is not restricted to use for patients with an eosinophilic asthma phenotype.

**Conclusion**

Asthma can be an extremely trying condition for patients to manage with a high healthcare burden. Pharmacists have the opportunity to impact patients through knowledge and education about available products and understanding about how prescribers may approach the management of asthma in their patients. Although treatment guidelines have remained consistent in recent years, there are new medications and devices emerging to enhance efficacy and safety of our therapeutic options. It is important that pharmacists are familiar with these new products and devices so that patients can be appropriately counseled regarding administration and drug information pertinent to their care. Currently, many of the new products emerging are utilizing new mechanisms of treatment. Although newer monoclonal antibody biologies have focused on patients with severe asthma to this point, there may be opportunities in the future for expanded use.

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**Disclosure:** The authors declare no real or potential conflicts of interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts and honoraria.

**References**


Assessment Questions

1. Which of the following risk factors are associated with poor asthma control?
   a. Assessment of inhaler technique
   b. High FEV1
   c. Infrequent SABA use
   d. Obesity

2. According to GINA 2018, patients with moderate severity asthma would be indicated for what step of therapy?
   a. STEP 1
   b. STEP 2
   c. STEP 3
   d. STEP 4
   e. STEP 5

3. True or False: The Respliclick® inhaler device should be used with a spacer.
   a. True
   b. False

4. Which of the following is a key difference between the Breo Ellipta and Advair Diskus devices?
   a. Breo Ellipta™ is an MDI while Advair Diskus® is a DPI
   b. Breo Ellipta™ requires priming while Advair Diskus® does not require priming
   c. Breo Ellipta™ is dosed once daily while Advair Diskus® is dosed twice daily
   d. Breo Ellipta™ does not require priming while Advair Diskus® does require priming
   e. Patient should rinse their mouth after using Breo Ellipta™ but do not have to rinse after using Advair Diskus

5. The recommended dosing of Spiriva Respimat® for the treatment of moderate-to-severe asthma is:
   a. 1.25 mcg/act 1 puff by mouth once daily
   b. 1.25 mcg/act 2 puffs by mouth once daily
   c. 2.5 mcg/act 1 puff by mouth once daily
   d. 2.5 mcg/act 2 puffs by mouth once daily
   e. 1.25 mcg/act 1 puff by mouth twice daily

6. Primatene® Mist is an OTC product reserved for use in the treatment of asthma as:
   a. A reliever medication for mild asthma symptoms
   b. A reliever medication for severe asthma exacerbations
   c. A controller medication for mild asthma symptoms
   d. A controller medication for moderate asthma symptoms
   e. A controller medication for moderate asthma symptoms

AP is a 22-year-old male with diagnosed “severe asthma”. He is currently taking Breo Ellipta™ 25mcg/ 200 mcg and using one inhalation daily. Recently he has been having 3-4 exacerbations per week that have required use of a reliever medication. His doctor measured his serum-eosinophil level and determined that it was “not-elevated”. He is not currently using any other medications besides the Breo Ellipta™ and his reliever inhaler. AP is most concerned about having to use another inhaler to control his symptoms and would prefer another route of administration if possible. Which of the following would be the most appropriate add-on therapy for AP?
   a. Primatene® Mist
   b. Montelukast
   c. Dupilumab
   d. Benralizumab
   e. Theophylline
   f. Sipra Respimat®

8. Among the new and emerging therapeutic agents for the control and relief of asthma symptoms, which of the following serves as a controller treatment option for patients without the eosinophilic phenotype?
   a. Primatene® Mist
   b. Dupilumab
   c. Tezepelumab
   d. Benralizumab

9. Did the activity meet the stated learning objectives? (If you answer no, please email sarahs@pswi.org to explain)
   a. Yes
   b. No

10. On a scale of 1 – 10 (1-no impact; 10-strong impact), please rate how this program will impact the medication therapy management outcomes or safety of your patients.

11. On a scale of 1 – 10 (1-did not enhance; 10-greatly enhanced), please rate how this program enhanced your competence in the clinical areas covered.
12. On a scale of 1 – 10 (1-did not help; 10-great help), please rate how this program helped to build your management and leadership skills.

13. How useful was the educational material?
   a. Very useful
   b. Somewhat useful
   c. Not useful

14. How effective were the learning methods used for this activity?
   a. Very effective
   b. Somewhat effective
   c. Not effective

15. Learning assessment questions were appropriate.
   a. Yes
   b. No

16. Were the authors free from bias?
   a. Yes
   b. No

17. If you answered “no” to question 16, please comment (emailinfo@pswi.org).

18. Please indicate the amount of time it took you to read the article and complete the assessment questions.

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