

Biologic Therapies for Moderate to Severe Asthma in the Pediatric Population: A Practice Update

SAGE Open Nursing
Volume 9: 1–5
© The Author(s) 2023
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/23779608231154041
journals.sagepub.com/home/son



Concettina Tolomeo, DNP, MBA, APRN, FNP-BC, AE-C¹ 

Abstract

Introduction: Asthma is a common childhood condition. Up until recent years, the mainstay of long-term control treatment has been inhaled corticosteroids. While inhaled corticosteroids are very effective for most children with asthma, with the introduction of biologic therapies, additional options now exist for children with uncontrolled moderate to severe asthma.

Purpose: The purpose of this Practice Update is to provide nursing professionals with a summary of the biologic therapies currently available for the pediatric population and, to describe when they are indicated for inclusion in the plan of care for children with moderate to severe asthma.

Conclusion: By properly diagnosing asthma, and, selecting and administering appropriate asthma therapies, nursing professionals can help children with moderate to severe asthma lead healthy and active lives.

Keywords

asthma, biologics, pediatrics/childhood

Received 26 August 2022; revised 4 December 2022; accepted 9 January 2023

Introduction

Asthma is a chronic pulmonary condition characterized by airway inflammation and hyperresponsiveness (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2007). Although asthma is more prevalent in adults, it is a common childhood condition. In 2020, 5.8% of children under the age of 18, in the United States, had asthma (Centers for Disease Control and Prevention, N.D.c). Unfortunately, when not well controlled, in addition to the disruptions caused in daily life, asthma can lead to significant morbidity and mortality as well as a disproportionate use of healthcare services (McGregor et al., 2019). Between 2018 and 2020, approximately 44% of children had asthma that was not well controlled (Centers for Disease Control and Prevention, N.D.e). In 2016, roughly 50% of children with asthma experienced at least one asthma exacerbation that same year. Asthma exacerbations result in missed school days, emergency department visits, hospitalizations, and death. In 2013, there were 13.8 million missed school days among school-aged children with asthma (Centers for Disease Control and Prevention, N.D.a). From 2016 to 2018, nearly two times as many children, as compared to

adults, experienced an emergency department or urgent care visit within the last year. Furthermore, in 2019, the rate of hospital admissions in children <18 years of age, per 10,000 population, was 8.8 (Centers for Disease Control and Prevention, N.D.d). While asthma-related deaths are lower than they were in the past, they still occur. From 2016 to 2018, the mortality rate for children was 2.7 per million (Pate et al., 2021). In 2013, direct costs (pharmacy, ambulatory, and hospital) related to pediatric asthma were \$13.8 billion (Perry et al., 2018). Based on these sobering numbers, it is easy to see that the cost of uncontrolled asthma in the pediatric population in the United States is significant from both a financial and a health perspective. Therefore, treating asthma to control its symptoms and prevent a decline in lung function is of paramount

¹Yale University, School of Medicine, Section of Pediatric Pulmonology, Allergy, Immunology, and Sleep Medicine, New Haven, CT, USA

Corresponding Author:

Concettina Tolomeo, DNP, APRN, FNP-BC, AE-C, Yale University, School of Medicine, Section of Pediatric Pulmonology, Allergy, Immunology, and Sleep Medicine, New Haven, CT, USA.
Email: tina.tolomeo@yale.edu



importance. Today there are novel biologic therapies that specifically target inflammatory mediators. These therapies allow for a more personalized approach to asthma treatment than conventional medications. As such, it is imperative that there is an increased awareness of the condition and emerging therapies so that children can have access to proper diagnosis and treatment of this common disease. The purpose of this Practice Update is to provide nursing professionals with a summary of the biologic therapies currently available for the pediatric population and, to describe when they are indicated for inclusion in the plan of care for children with moderate to severe asthma. Although other asthma medications are critical to the successful management of children with asthma, they are not the focus of this Practice Update.

Brief Review/Update

Asthma Management

Pediatric asthma is classified as intermittent, mild persistent, moderate persistent, or severe persistent (National Asthma Education and Prevention Program, 2007). Treatment of asthma is based on the severity level. Approximately 60% of children with asthma have persistent asthma (Centers for Disease Control and Prevention, N.D.b). There are several definitions of severe persistent asthma that have been documented in the literature (Votto et al., 2021). As such, it has been difficult to determine what percent of children have severe persistent asthma, though the estimates are low. The majority of children have mild to moderate persistent asthma (Rusconi et al., 2018). Pediatric asthma treatment consists of assessment and monitoring, education, environmental control measures, and medication therapy (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2007).

There are two broad medication therapy categories in asthma care, quick-relief, and long-term control medications. Quick-relief medications are used to gain fast control of active symptoms. Based on the child's age, there are two preferred quick-relief options, they are Albuterol and combination therapy with an inhaled corticosteroid and Formoterol (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2020). Long-term control therapy is used to control symptoms of asthma and prevent exacerbations, emergency department visits, and hospitalizations associated with poorly controlled asthma. The most common long-term control treatment is the inhaled corticosteroid. Examples of inhaled corticosteroids include Budesonide, Fluticasone, and Mometasone. Depending on the severity of asthma, inhaled corticosteroids are used alone or as a combination product with a long-acting bronchodilator. These combination products include Budesonide/Formoterol, Fluticasone Propionate/Salmeterol, and Mometasone/Formoterol to name a few. Other long-term control medications include leukotriene modifiers, mast cell

stabilizers, and the most recent additions, the biologics. Biologic therapies have the ability to target specific pathways that lead to inflammation and subsequent symptoms of asthma (McGregor et al., 2019). Although most patients can be controlled on traditional long-term control therapies, there remains a subset of patients with asthma who are not well controlled. Biologic therapies have been found to reduce asthma exacerbations and the use of oral corticosteroids as well as improve lung function and quality of life (McGregor et al., 2019). Biologic therapies include immunoglobulin E (IgE) antagonists, interleukin (IL)-4/13 antagonists, IL-5 antagonists, and a thymic stromal lymphopoietin (TSLP) antagonist (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2020). The five biologics currently indicated for patients under the age of 18 will be presented in this Practice Update.

Biologic Options

The biologic therapies presented below are approved in the United States for children with either moderate or severe asthma (Table 1). In research studies, all five therapies have demonstrated benefits, when used as indicated, in pediatric patients, adult patients, or both.

Omalizumab is the oldest biologic available in the pediatric population. It is an anti-IgE therapy. It binds to circulating IgE, blocking attachment to the IgE receptor and thus preventing the release of inflammatory mediators (Russo et al., 2021; Votto et al., 2021). Omalizumab is indicated for children ≥ 6 years of age with uncontrolled moderate to severe allergic asthma, an IgE of 50 to 1,500 IU/ml, and sensitivity to aeroallergens (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2020; Russo et al., 2021; Votto et al., 2021). Studies have revealed a decrease in asthma exacerbations, hospitalizations, oral corticosteroids, and bronchodilator use and, an increase in quality of life with the use of Omalizumab (Bush, 2020; Russo et al., 2021; Votto et al., 2021). Omalizumab is administered subcutaneously every two to four weeks depending on the child's IgE level at the initiation of therapy and, the child's current weight. The dose is also dependent on the child's IgE level at the initiation of therapy and the child's current weight (Russo et al., 2021; Votto et al., 2021). The lowest dose is 75 mg and the highest dose is 375 mg. Dosing charts can be found at: <https://www.xolairhcp.com/starting-treatment/dosing.html>. Side effects of Omalizumab include local injection site reaction, pain, and immediate or delayed anaphylaxis (Russo et al., 2021; Votto et al., 2021). Considering the potential for anaphylaxis, all children on Omalizumab should have a prescription for subcutaneous Epinephrine and be trained in its use.

Mepolizumab is an anti-IL-5 therapy. It attaches to and inhibits IL-5 (Russo et al., 2021; Votto et al., 2021). It is indicated for children ≥ 6 years of age with severe, uncontrolled eosinophilic asthma and a blood eosinophil count of ≥ 150

Table 1. Biologic Therapies for Children with Asthma.

Biologic	Type	Indication	Route	Frequency
Benralizumab	Anti-IL-5R α	≥ 12 years of age with uncontrolled, severe eosinophilic asthma and a blood eosinophil count of ≥ 150 cells/ μ L	Subcutaneously	Every four weeks for the first three doses and then every eight weeks
Dupilumab	Anti-IL-4R α	≥ 6 years of age with uncontrolled, moderate to severe eosinophilic asthma and a blood eosinophil count of ≥ 150 cells/ μ L	Subcutaneously	Every 2 weeks
Mepolizumab	Anti-IL-5	≥ 6 years of age with severe, uncontrolled eosinophilic asthma and a blood eosinophil count of ≥ 150 cells/ μ L	Subcutaneously	Every 4 weeks
Omalizumab	Anti-IgE	≥ 6 years of age with uncontrolled moderate to severe allergic asthma, an IgE of 50 to 1500 IU/mL, and sensitivity to aeroallergens	Subcutaneously	Every 2 to 4 weeks
Tezepelumab	Anti-TSLP	≥ 12 years of age with uncontrolled severe asthma	Subcutaneously	Every 4 weeks

Note. IL = interleukin; IgE = immunoglobulin E; TSLP = thymic stromal lymphopoietin.

cells/ μ L (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2020; Russo et al., 2021; Votto et al., 2021). Studies have revealed a decrease in asthma exacerbations, hospitalizations, and oral corticosteroid use with the use of Mepolizumab (Bush, 2020). Mepolizumab is administered subcutaneously every four weeks. For children 6 to 11 years of age, the dose is 40 mg. For children 12 years of age and older, the dose is 100 mg. Side effects include local injection site reactions, headaches, fatigue, and respiratory infections (Russo et al., 2021; Votto et al., 2021).

Benralizumab is an anti-IL-5R α therapy. It attaches to IL-5R α and decreases eosinophils (Russo et al., 2021; Votto et al., 2021). It is indicated for children ≥ 12 years of age with uncontrolled, severe eosinophilic asthma and a blood eosinophil count of ≥ 150 cells/ μ L (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2020; Russo et al., 2021; Votto et al., 2021). Studies have revealed a decrease in asthma exacerbations and symptoms, and improved pretreatment forced exhaled volume in one second (Russo et al., 2021; Votto et al., 2021). Benralizumab is administered subcutaneously in a dose of 30 mg every four weeks for the first three doses and then every eight weeks. Common side effects include sore throat and headache (AstraZeneca, 2021a).

Dupilumab is an anti-IL-4R α . It blocks both the IL-4 and the IL-13 receptors (Russo et al., 2021; Votto et al., 2021). It is indicated for children ≥ 6 years of age with uncontrolled, moderate to severe eosinophilic asthma and a blood eosinophil count of ≥ 150 cells/ μ L (Global Initiative for Asthma, 2022; National Asthma Education and Prevention Program, 2020; Russo et al., 2021; Votto et al., 2021). Studies have revealed a decrease in asthma exacerbations and oral steroid use as well as an improvement in spirometry (Votto et al., 2021). Benefits were particularly significant in patients with a high (≥ 25 ppb) fractional exhaled nitric oxide (FENO) and high (≥ 300 cells/ μ L) eosinophil count (Votto et al., 2021). Dupilumab has also shown efficacy in patients with

nasal polyposis, chronic rhinosinusitis, atopic dermatitis, and eosinophilic esophagitis (Russo et al., 2021). Dupilumab is administered subcutaneously every two weeks. For children on chronic oral steroid therapy or with comorbid moderate-to-severe dermatitis, the recommended dose is 600 mg in the first week followed by 300 mg every two weeks. For all others, the recommended dose is 400 mg in the first week followed by 200 mg every two weeks. Side effects include local injection site reactions, respiratory infections, and transient eosinophilia (Russo et al., 2021; Votto et al., 2021).

Tezepelumab is the newest biologic to receive approval for children. It is an anti-TSLP. It attaches to the TSLP to reduce cytokines associated with inflammation. It is indicated for children ≥ 12 years of age with uncontrolled severe asthma (Global Initiative for Asthma, 2022; Russo et al., 2021). Studies have revealed a decrease in asthma exacerbations and, an increase in asthma control, spirometry, and quality of life. Benefits were particularly significant in patients with a high (≥ 25 ppb) FENO and high (≥ 300 cells/ μ L) eosinophil count. Tezepelumab is administered subcutaneously in a dose of 210 mg every 4 weeks (Russo et al., 2021). The most common side effects include joint pain, sore throat, and back pain (AstraZeneca, 2021b).

Selecting a Biologic

If a child continues to experience exacerbations on preferred treatment, they may be candidates for a biologic medication. Aside from age of the child, to determine if biologic therapy is right for your patient, you must first determine asthma severity and control and, rule out any other possible reasons for lack of control, such as a comorbid condition, nonadherence to therapy, or inappropriate inhaler technique. Once it has been confirmed that your patient has uncontrolled moderate or severe asthma, it must be determined if your patient has allergic or eosinophilic asthma by assessing IgE levels, eosinophil counts, and FENO (Global Initiative for Asthma, 2022).

For allergic uncontrolled asthma, Omalizumab would be the option of choice. If the patient has eosinophilic asthma, one of the other biologic therapies can be considered. If the patient has a high eosinophil count or FENO, Dupilumab and Tezepelumab would be good options (Global Initiative for Asthma, 2022; Russo et al., 2021; Votto et al., 2021). Furthermore, if the patient has nasal polyposis, chronic rhinosinusitis, atopic dermatitis, or eosinophilic esophagitis, Dupilumab would be a good first choice (Russo et al., 2021). Other determining factors include the frequency of administration and how the therapy will fit the child's and family's lifestyle. A recent study, conducted at the beginning of the COVID-19 pandemic, demonstrated that children can safely receive Omalizumab and Mepolizumab at home with the use of virtual video monitoring (Makhecha et al., 2021). While the use of video monitoring is not required, Omalizumab, Mepolizumab, Benralizumab, and Dupilumab are available in prefilled syringes to be administered at home after an initial dose has been administered and tolerated in a controlled setting. Additionally, the child/parent/guardian must be adequately trained in and comfortable with the administration of the medication in the home setting prior to prescribing it for home use. Home use is more convenient than going to an office setting every 2 to 8 weeks and thus has the potential to improve adherence to therapy. Lastly, it is important to consider cost. All five of the biologics have patient assistance programs that can be accessed via their websites.

- Omalizumab: <https://www.xolairhcp.com/access-resources/financial-assistance.html>.
- Mepolizumab: <https://www.nucala.com/severe-asthma/savings-and-support/co-pay-program/>.
- Benralizumab: <https://www.fasenra.com/savings-and-support.html>.
- Dupilumab: <https://www.dupixent.com/support-savings/copy-card>.
- Tezepelumab: <https://www.tezspirehcp.com/patient-support-program.html>.

Importance to Nursing Profession

Knowledge regarding emerging therapies is important for all areas of the nursing profession. In education, it is imperative that nursing students receive training and information regarding the most up-to-date therapies they will encounter during their clinical rotations and in practice. Having this baseline knowledge will prepare them to care for their patients and communicate with other healthcare professionals. Clinically, whether you are an advanced practice, registered, or licensed practical nurse caring for children, it is important to remain knowledgeable about the latest treatments for common childhood conditions. Knowledge regarding medication indications, doses, side effects, and assistance programs will help advanced practice nurses choose the right treatment to

control their patients' asthma. This information will also allow registered and licensed practical nurses to safely administer the medications, monitor for side effects, and educate patients and their families. Finally, an understanding of the current state of biologic therapies in childhood asthma may prompt nurse researchers to participate in, and/or lead research studies in an effort to further advance evidence-based practice in this important area.

Conclusion

Childhood asthma remains a common condition that unfortunately still leads to emergency department visits, hospitalizations, and even death. Children with uncontrolled asthma have more morbidity and mortality related to their disease. Although at this time asthma cannot be cured, it can be controlled. Biologic therapies can target specific pathways that contribute to the pathogenesis and symptoms of asthma. Staying up to date with emerging therapies will allow children with asthma to receive the latest evidence-based treatments to manage their condition and help them lead normal lives with asthma.

Declaration of Conflicting Interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Concettina Tolomeo  <https://orcid.org/0000-0002-7739-0890>

References

- AstraZeneca (2021a). *Benralizumab: Fasenra prescribing information*. AstraZeneca.
- AstraZeneca. (2021b). *Tezepelumab: Tezspire full prescribing information*. AstraZeneca.
- Bush, A. (2020). Which child with asthma is a candidate for biological therapies? *Journal of Clinical Medicine*, 9(4), Article 1237. <https://doi.org/10.3390/jcm9041237>
- Centers for Disease Control and Prevention (CDC) (N.D.a). Asthma-related missed school days among children aged 5–17 years. https://www.cdc.gov/asthma/asthma_stats/missing_days.htm
- Centers for Disease Control and Prevention (CDC) (N.D.b). Asthma severity among children with current asthma. https://www.cdc.gov/asthma/asthma_stats/severity_child.htm
- Centers for Disease Control and Prevention (CDC) (N.D. c). Asthma surveillance data. <https://www.cdc.gov/asthma/asthmadata.htm>
- Centers for Disease Control and Prevention (CDC) (N.D.d). 2019 healthcare use data. https://www.cdc.gov/asthma/healthcare-use/2019/table_b.html
- Centers for Disease Control and Prevention (CDC) (N.D.e). Uncontrolled asthma among children with current asthma,

- 2018–2020. https://www.cdc.gov/asthma/asthma_stats/uncontrolled-asthma-children-2018-2020.htm
- Global Initiative for Asthma (2022). Global strategy for asthma management and prevention (2022 update). <https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf>
- Makhecha, S., Jamalzaeh, A., Irving, S., Hall, P., Sonnappa, S., Saglani, S., Bush, A., & Fleming, L. (2021). Pediatrics severe asthma biologics service: From hospital to home. *Archives of Disease in Childhood*, *106*, 900–902. <https://doi.org/10.1136/archdischild-2020-320626>
- McGregor, M. C., Krings, J. G., Nair, P., & Castro, M. (2019) Role of biologics in asthma. *American Journal of Respiratory and Critical Care Medicine*, *199*(4), 433–445. <https://doi.org/10.1164/rccm.201810-1944CI>
- National Asthma Education and Prevention Program (2007). Third expert panel on the diagnosis and management of asthma. National Heart, Lung, and Blood Institute, Report No. 07-4051. https://www.nhlbi.nih.gov/sites/default/files/media/docs/EPR-3_Asthma_Full_Report_2007.pdf.
- National Asthma Education and Prevention Program (2020). 2020 focused updates to the asthma management guidelines. National Heart, Lung, and Blood Institute, NIH Publication No. 20-HL-8140. [C:/Users/ct36/Downloads/AsthmaManagementGuidelinesReport-2-4-21%20\(3\).pdf](C:/Users/ct36/Downloads/AsthmaManagementGuidelinesReport-2-4-21%20(3).pdf).
- Pate, C. A., Zahran, H. S., Qin, X., Johnson, C., Hummelman, E., & Malilay, J. (2021). Asthma surveillance—United States, 2006–2018. *MMWR Surveillance Summaries*, *70*(No. SS-5):1–32. https://www.cdc.gov/mmwr/volumes/70/ss/ss7005a1.htm?s_cid=ss7005a1_w
- Perry, R., Braileanu, G., Palmer, T., & Stevens, P. (2018). The economic burden of pediatric asthma in the United States: Literature review of current evidence. *Pharmacoeconomics*, *37*(2), 155–167. <https://doi.org/10.1007/s40273-018-0726-2>
- Rusconi, F., Fernandes, R. M., Pinenburg, M. W. H., & Grigg, J. (2018). The Severe Paediatric Asthma Collaborative in Europe (SPACE) ERS Clinical Research Collaboration: Enhancing participation of children with asthma in therapeutic trials of new biologics and receptor blockers. *European Respiratory Journal*, *52*, Article 1801665. <https://doi.org/10.1183/13993003.01665-2018>
- Russo, D., DiFilippo, P., Attanasi, M., Lizzi, M., DiPillo, S., & Chiarelli, F. (2021). Biologic therapy and severe asthma in children. *Biomedicine*, *9*, Article 760. <https://doi.org/10.3390/biomedicine9070760>
- Votto, M., DeFilippo, M., Licari, A., Marseglia, A., DeAmici, M., & Marseglia, G. L. (2021). Biological therapies in children and adolescents with severe uncontrolled asthma: A practical review. *Biologics: Targets and Therapy*, *15*, 133–142. <https://doi.org/10.2147/BTT.S252574>