IMPORTANT REMINDER
This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description
Xolair® (omalizumab) is a human monoclonal antibody used in allergic (extrinsic) asthma and chronic idiopathic urticaria (hives), to bind IgE. In patients with asthma, omalizumab prevents IgE from attaching to mast cells, therefore preventing the activation of the allergic cascade and decreasing airway inflammation. In patients with urticaria, omalizumab lowers free IgE levels and leads to IgE receptor downregulation; however, it is unknown exactly how omalizumab reduces hives and itching.
Policy/Criteria

I. Most contracts require prior authorization approval of omalizumab prior to coverage. Omalizumab may be considered medically necessary for the following diagnoses, when medical criteria below are met.

A. Asthma, when all criteria 1 through 6 below are met.
   1. Patient is currently followed by an asthma specialist (allergist, immunologist, or pulmonologist).
      AND
   2. Positive skin prick test or in-vitro specific IgE test (such as RAST, MAST, FAST, ELISA) to one or more allergens, (or is currently receiving specific immunotherapy like allergy shots) which support the patient's clinical history.
      AND
   3. Total serum IgE level is one of the following (a, b., c., or d. below):
      a. For patients >50 kg: 30 to 700 IU/ml.
      b. For patients >40 to 50 kg: 30 to 900 IU/ml.
      c. For patients >30 to 40 kg: 30 to 1,100 IU/ml.
      d. For patients 20 to 30 kg: 30 to 1,300 IU/ml.
      AND
   4. Clinical documentation of poor asthma control or recurrent exacerbation requiring additional medication treatment:
      - Additional medical treatment may include any of the following: treatment with oral corticosteroids, ER visits, hospitalizations, or frequent office visits.
      - Poor asthma control may include (but is not limited to) clinical documentation of limitation of activities of daily living (ADLs), nighttime awakening, or dyspnea.
      - Recurrent exacerbation is defined as 2 or more acute exacerbations in a 12-month period.
      AND
   5. Clinical documentation that patient is compliant with high-dose inhaled corticosteroids (ICS) and long-acting inhaled beta-2 agonists (LABA) (Step 5 of the National Asthma Treatment Guidelines) and use of oral corticosteroids for exacerbation unless contraindicated.
      AND
   6. Underlying conditions or triggers for asthma or pulmonary disease are being maximally managed.

B. Chronic Idiopathic/Spontaneous urticaria, when ALL criteria 1 through 6 below are met:
   1. Patient is currently followed by a specialist in allergy/immunology, dermatology, or pulmonary medicine.
      AND
   2. An evaluation has been performed to rule out other causes of urticaria and identify potential triggers.
AND
3. Clinical documentation of spontaneous urticarial flares, in the absence of potential triggers (despite avoidance of triggers).

AND
4. Underlying conditions or identified triggers for urticaria are being maximally managed.

AND
5. Clinical documentation of functional impairment due to poor urticaria control or exacerbations, which may include (but is not limited to) documentation of limitation of activities of daily living (ADLs), such as missing school or work or insomnia due to itching.

AND
6. Clinical documentation that patient is compliant with H1 antihistamines (see Appendix 1) at the maximally tolerated doses, unless contraindicated

II. Administration, Quantity Limitations, and Authorization Period
A. OmedaRx does not consider omalizumab to be a self-administered medication.
B. When prior authorization is approved, omalizumab may be authorized as follows:
   1. **Asthma:** up to 375mg (three - 150 mg vials) every 2 weeks for up to 6 months.
   2. **Idiopathic urticaria:** up to 300 mg (two- 150 mg vials) every 4 weeks for up to 3 months.
C. Authorization may be reviewed at least every 6 months to confirm that current medical necessity criteria are met and that the medication is effective defined as sustained clinical improvement from reduced asthma/urticaria symptoms (such as reduced missed days from work or school) or stable asthma control.

III. Omalizumab is considered not medically necessary when used for allergic rhinitis.

IV. Omalizumab is considered investigational when used for all other conditions, including, but not limited to:
   A. Allergic bronchopulmonary aspergillosis (ABPA)
   B. Atopic dermatitis
   C. Eosinophilic esophagitis
   D. Hyperimmunoglobulin E syndrome (including Job’s syndrome)
   E. Peanut or other food allergies.
   F. Urticaria, non-idiopathic (e.g. cold-induced)
Position Statement

Summary

- Omalizumab is a monoclonal antibody that reduces the levels of circulating IgE and inhibits binding of IgE to mast cells, to prevent the activation of the allergic cascade and decrease inflammation.
- It is approved for adolescents (12 years and above) and adults with moderate-to-severe persistent allergic asthma inadequately controlled with inhaled corticosteroids, as well as antihistamine-refractory chronic idiopathic urticaria.
- Omalizumab is effective in reducing asthma exacerbations and need for inhaled steroids in patients with asthma that is triggered by allergens. Omalizumab has not been proven to be safer or more effective than preferred options recommended in treatment guidelines, nor in patients with less severe asthma/urticaria or non-allergic asthma.
- Omalizumab may have some impact on severe, chronic refractory idiopathic urticaria; however, the clinical benefit is uncertain, the dose is not well-established and there are other treatment options. The goal of therapy is to decrease functional impairment due to itching, hives and other related symptoms, such as missed days from work and/or school.
- For both asthma and chronic urticaria, omalizumab has not been proven to be safer or more effective than preferred options recommended in treatment guidelines, nor in patients with less severe asthma/urticaria, non-allergic asthma, or non-idiopathic urticaria (urticaria with a clearly defined underlying cause).

* Allergen control and high-dose inhaled corticosteroids in combination with a long-acting inhaled beta-agonist (STEP 5 therapy) are effective in the treatment of many patients with persistent asthma, along with leukotriene inhibitors and oral steroids for exacerbations.

* Standard of care for chronic urticaria includes identification and elimination of the underlying aggravating triggers followed by use of antihistamines. Other potential therapies include leukotriene antagonists, cyclosporine, dapsone, other oral DMARDs, and corticosteroids. All patients in clinical trials of omalizumab for urticaria were refractory to antihistamines.

- Omalizumab has not been proven to be safer or more effective than other treatment options for seasonal and perennial allergic rhinitis symptoms, such as nasal corticosteroids, antihistamines, or allergen desensitization therapy.
- Omalizumab is not considered a self-injectable medication for safety reasons; therefore, it is only coverable under the medical benefit. Medical observation for hypersensitivity reactions is necessary following omalizumab administration.
- Omalizumab may be covered for up to 375 mg every two weeks for asthma and 300 mg every four weeks for chronic idiopathic urticaria, the dosing at which it has been shown to be safe and effective.
Clinical Efficacy

**ASTHMA**

- Omalizumab increases the number of asthma patients who are able to reduce or withdraw their inhaled steroids and is effective in reducing asthma. [1-4]
- There are no available data demonstrating that omalizumab is superior to preferred options recommended in treatment guidelines for moderate-to-severe persistent asthma. [5-7]
- Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements (multiple cytokines and mediators, as well as potentially IgE-mediated events involving mast cells and basophils) play a role (in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils and epithelial cells).
- IgE may be in the inflammatory cascade of some events leading to asthmatic airway inflammation; it is only one part of the picture.
- National Heart, Lung, and Blood Institute (NHLBI) recommended first-line STEP5 asthma therapies for persistent asthma including use of as-needed short-acting beta-agonists (SABAs), high-dose inhaled corticosteroids (ICS), and inhaled long-acting beta-agonists (LABAs), along with strict allergen (environmental) control. Oral corticosteroids are recommended for exacerbations, as well as STEP 6 therapy. [6]
- Optimal clinical response to omalizumab requires strict compliance with dosing, as there is a 6 to 12 week lag before beneficial effects are apparent. (Effects are not immediate and explain the various phases that are included in study protocols.)

The efficacy of omalizumab in patients with a history of smoking has not been established (patients with a smoking history in the previous two years or who had a previous history of greater than or equal to 10 pack-years were excluded from omalizumab clinical trials). [8]

- Although preliminary results are promising, there is no conclusive evidence that omalizumab is effective in patients with non-allergic (nonatopic) asthma, based on one small proof-of-concept trial. [9]

**Total IgE Levels**

- Omalizumab (Xolair) is only indicated in patients with elevated IgE levels and is dosed according to IgE levels between 30 to 700 IU/ml. [10] There is no established dose or benefit for IgE levels outside of this range.
- Efficacy and dosing of omalizumab in asthma patients (> 50 kg) with IgE levels less than 30 or greater than 700 have not been established. [10] The majority of data on the use of omalizumab (Xolair) in patients with baseline IgE <30 or >700 IU/ml are limited to case reports with inconsistent results of effectiveness.
- There is evidence to support the safety and efficacy of omalizumab in patients less than 12 years old with a baseline IgE as follows:
  - 20 to 30 kg: baseline IgE of 30 to 1,300 IU/ml
  - >30 to 40 kg: baseline IgE of 30 to 1,100 IU/ml
  - >40 to 50 kg: baseline IgE of 30 to 900 IU/ml
- Monitoring IgE levels after administration of omalizumab are problematic, as IgE levels post-administration measure both bound and unbound (free) IgE.
CHRONIC IDIOPATHIC URTICARIA (Also known as “Chronic Spontaneous Urticaria”)

- Omalizumab may reduce urticaria severity, as measured by itch-severity score, in patients with chronic idiopathic urticaria who remained symptomatic despite use of H1-antihistamine therapy. However, omalizumab has not been proven to eliminate itching or improve functional impairment due to urticaria symptoms. [11-14]
- The efficacy or safety of omalizumab in other types of urticaria with a clearly defined cause, such as physical urticaria (e.g. “cold” urticaria), urticarial vasculitis, or contact urticaria, has not been established. [13-15] Patients with a clearly defined cause for urticaria, such as physical cause, were excluded from clinical trials. [11-14]
- Omalizumab has only been studied as add-on therapy. All patients in clinical trials of omalizumab for chronic urticaria were refractory to antihistamines. [13]
- However, omalizumab has not been compared to the many other available therapies for antihistamine-refractory urticaria. Therefore it is unknown if omalizumab is superior to these less-costly alternatives.
- IgE levels are not measured nor used as a marker for omalizumab therapy with urticaria.
- Standard of care includes identification and elimination of the underlying aggravating triggers followed by use of antihistamines, which are FDA-approved for treatment of urticaria, and may be used at doses exceeding the manufacturer’s recommended dosages. [13]
- Second-line treatment options for antihistamine-refractory urticaria include H2-antihistamines (e.g. ranitidine, famotidine), leukotriene antagonists, cyclosporine, dapsone, other oral DMARDs/anti-inflammatories (methotrexate, sulfasalazine), and corticosteroids. The guidelines acknowledge the evidence supporting the use of these second-line therapies is of lower quality; however their costs and safety profiles should be considered when choosing therapies. [13]

Nomenclature

- The terms “chronic urticaria” (CU), “chronic spontaneous urticaria” (CSU) and “chronic idiopathic urticaria” (CIU) are used interchangeably, but are a frequent cause of severe chronic urticaria, lasting greater than 6 weeks. [13] However, in clinical trials, all patients had CIU symptoms for at least 6 months. [9-12,14] The diagnosis of “chronic idiopathic urticaria” requires exclusion of physical causes as a main cause of the urticaria symptoms, such as dermatographism (firm stroking), delayed pressure urticaria (pressure), cold urticaria (cold), solar urticaria (exposure to sun), or vibratory urticaria (vibration), as well as other causes [aquagenic urticaria (water exposure), cholinergic urticaria (heat, stress, exercise), exercise-induced anaphylaxis/urticaria, contact with urticariogenic substances]. Urticaria despite avoidance of triggers is a hallmark feature of CIU/CSU. [13]
- A subset of patients with a diagnosis of chronic idiopathic urticaria may have autoimmune urticaria, which can be associated with some type of trigger which can aggravate symptoms but is not the main cause of CU symptoms. Aggravating triggers may include but are not limited to extreme hot or cold, and irritation from clothing. [13] Primary treatment for CU should include aggravating trigger control and histamine blockade. Refractory patients may be responsive to omalizumab. [11-13]
OTHER USES:

There is insufficient evidence to support the use of omalizumab in a variety of other conditions, including, but not limited to, allergic bronchopulmonary aspergillosis (ABPA), atopic dermatitis, cutaneous mastocytosis, eosinophilic esophagitis, hyperimmunoglobulin E syndrome (Job’s syndrome), other types of urticaria, or peanut or other food allergies. The evidence is limited to low level evidence, such as case series or pilot trials. [15-26]

- Phase 2 results suggesting benefits of another anti-IgE compound-TNX-901 for treatment of peanut allergy cannot be extrapolated to the use of omalizumab to protect against anaphylaxis in patients with peanut allergy. [16]
- Omalizumab reduces seasonal and perennial allergic rhinitis symptoms, [17-19] but has not been shown to have better efficacy than first-line alternatives, such as nasal corticosteroids, antihistamines, or allergen desensitization therapy.
- One small trial found no benefit of omalizumab in patients with eosinophilic esophagitis. [25]
- The one small crossover trial (n=13) found a reduction in exacerbations over a 4-month period in patients with ABPA with use of high-dose omalizumab (750 mg monthly) (p=0.048); however, the long-term clinical benefit is unknown. Additional research is needed to clarify the safety, efficacy, and optimal dosing of omalizumab for ABPA. [26]

Safety

- Omalizumab has a boxed warning for anaphylaxis. [10]
  * Anaphylaxis in patients after treatment with omalizumab. These reactions generally occur within two hours of receiving omalizumab.
  * Delayed anaphylaxis—with onset two to 24 hours or even longer—after receiving omalizumab treatment.
  * Anaphylaxis can occur after any dose.
  * It is recommended that patients be observed for at least two hours after omalizumab is administered.
- The FDA long-term safety data that suggest a slightly elevated risk of cardiovascular and cerebrovascular adverse events. [27]

Dosing

- For asthma, omalizumab is given 150 to 375 mg every two to four weeks.
- Doses up to 300 mg every 4 weeks have been used for treatment of chronic urticaria. [38]
- Efficacy and dosing of omalizumab in asthma patients whose weight is outside the range provided in the standard dosing table for omalizumab has not been established (weight-IgE level combinations yielding doses greater than 750 mg every 4 weeks were excluded from clinical trials). [8,10]
# Appendices

## Appendix 1: Antihistamines

### H<sub>1</sub>-Antihistamines

**First Generation (non-selective, “sedating”)**
- brompheniramine
- chlorpheniramine (generic Chlor-Trimeton)
- clemastine (generic Tavist)
- cyproheptadine (generic Periactin)
- dextromethorphan
- diphenhydramine (generic Benadryl)
- hydroxyzine (generic Vistaril)

**Second Generation (peripherally-selective, “non-sedating”)**
- cetirizine (generic Zyrtec)
- desloratadine (Clarinex)
- fexofenadine (generic Allegra)
- levocetirizine (Xyzal)
- loratadine (generic Claritin)

### H<sub>2</sub>-Antihistamines

- cimetidine (generic Tagamet)
- famotidine (generic Pepcid)
- nizatidine (generic Avid)
- ranitidine (generic Zantac)
Appendices 2 to 5: National Heart, Lung and Blood Institute (NHLBI) Asthma Treatment Guidelines


Appendix 2: Stepwise Approach for Managing Asthma Long-Term in Children, age 0 to 4

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermittent Asthma</strong></td>
<td><strong>Persistent Asthma: Requiring Daily Medication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consult with asthma specialist if step 3 care or higher is required. Consider consultation at step 2.</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Preferred:**
- SABA PRN
- low-dose ICS
- medium-dose ICS
- high-dose ICS + LABA or montelukast
- high-dose ICS + LABA or montelukast or oral corticosteroids

**Alternative:**
- cromolyn or montelukast

**Each step: Patient education and environmental control.**

**Quick-Relief Medication**
- Should be available for all patients.
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms.
- With viral respiratory infection: SABA q 4–6 hours up to 24 hours (longer with physician consult). Consider short course of oral systemic corticosteroids if exacerbation is severe or patient has history of previous severe exacerbations.

Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy

Step up if needed (first, check adherence, inhaler technique, and environmental control)

Assess control

Step down if possible (and asthma is well controlled at least 3 months)

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 (See Appendix 4, for classification of ICS strength); LABA: inhaled long-acting beta2-agonist; SABA: inhaled short-acting beta2-agonist.

Notes:
- The stepwise approach is meant to assist, not replace, the clinical decision making 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.
- If clear benefit is not observed within 4–6 weeks and patient/family medication technique and adherence are satisfactory, consider adjusting therapy or alternative diagnosis.
- Studies on children 0–4 years of age are limited. Step 2 preferred therapy is based on Evidence A. All other recommendations are based on expert opinion and extrapolation from studies in older children.
# Appendix 3: Stepwise Approach for Managing Asthma Long-Term in Children, age 5 to 11

## Intermitent Asthma

### Persistent Asthma: Requiring Daily Medication

Consult with asthma specialist if step 3 care or higher is required. Consider consultation at step 2.

### Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have persistent, allergic asthma (see notes).

### Quick-Relief Medication

- Should be available for all patients.
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Caution: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
- Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy

## Preferred:

<table>
<thead>
<tr>
<th>Step 1</th>
<th>SABA PRN</th>
<th>low-dose ICS</th>
<th>low-dose ICS  + LABA, LTRA or theophylline</th>
<th>medium-dose ICS  + LABA</th>
<th>High-dose ICS  + LABA</th>
</tr>
</thead>
</table>

## Alternative:

<table>
<thead>
<tr>
<th>Step 1</th>
<th>cromolyn, LTRA, nedocromil, or theophylline</th>
<th>medium-dose ICS  + LTRA or theophylline</th>
<th>high-dose ICS  + LTRA or theophylline</th>
</tr>
</thead>
</table>

### High-dose ICS  + LABA  + oral corticosteroids

### High-dose ICS  + LTRA or theophylline  + oral corticosteroids

---

**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 (See Appendix 4, for classification of ICS strength); LABA: inhaled long-acting beta2-agonist; LTRA: leukotriene receptor antagonist (montelukast or zafirlukast); SABA: inhaled short-acting beta2-agonist.

**Notes:**

- The stepwise approach is meant to assist, not replace, the clinical decision making 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.
## Appendix 4: Stepwise Approach for Managing Asthma in Youths ≥ 12 years old and Adults

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermittent Asthma</strong></td>
<td><strong>Persistent Asthma: Requiring Daily Medication</strong></td>
<td>Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Preferred:

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent Asthma</td>
<td>Persistent Asthma: Requiring Daily Medication</td>
<td>Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Step 1**: SABA PRN
- **Step 2**: low-dose ICS
- **Step 3**: low-dose ICS + LABA
- **Step 4**: medium-dose ICS + LABA
- **Step 5**: High-dose ICS + LABA + oral corticosteroids
- **Step 6**: High-dose ICS + LABA + oral corticosteroids

### Alternative:

- **Step 1**: cromolyn, LTRA, nedocromil, or theophylline
- **Step 2**: low-dose ICS + LTRA, theophylline or zileuton
- **Step 3**: medium-dose ICS + LTRA, theophylline or zileuton
- **Step 4**: Consider omalizumab for patients who have allergies
- **Step 5**: Consider omalizumab for patients who have allergies

### Quick-Relief Medication

- **Step 1**: Should be available for all patients.
- **Step 2**: SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- **Step 3**: Caution: Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
- **Step 4**: Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term-control therapy

### Key:

- Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.
- The stepwise approach is meant to assist, not replace, the clinical decision making 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.
## Appendix 5: NHBLI Estimated Comparative Daily Dosages for Inhaled Corticosteroids (ICS) in Adults

<table>
<thead>
<tr>
<th>Drug</th>
<th><strong>Low Daily Dose</strong></th>
<th><strong>Medium Daily Dose</strong></th>
<th><strong>High Daily Dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Child 0–4 yo 5–11 yo ≥12 yrs</td>
<td>Child 0–4 yo 5–11 yo ≥12 yrs</td>
<td>Child 0–4 yo 5–11 yo ≥12 yrs</td>
</tr>
<tr>
<td>Beclomethasone HFA 40 or 80 mcg/puff</td>
<td>80–160 mcg</td>
<td>&gt;160–320 mcg</td>
<td>NA 320–480 mcg</td>
</tr>
<tr>
<td></td>
<td>80–240 mcg</td>
<td>240–480 mcg</td>
<td>NA &gt;480 mcg</td>
</tr>
<tr>
<td>Budesonide DPI 90, 180, 200 mcg/inhalation a</td>
<td>180–400 mcg</td>
<td>&gt;400–800 mcg</td>
<td>NA &gt;800 mcg</td>
</tr>
<tr>
<td></td>
<td>180–600 mcg</td>
<td>600–1,200 mcg a</td>
<td>&gt;1,200 mcg a</td>
</tr>
<tr>
<td>Budesonide Inhaled Inhalation suspension for nebulization</td>
<td>0.25–0.5 mg</td>
<td>&gt;0.5–1.0 mg</td>
<td>&gt;1.0 mg</td>
</tr>
<tr>
<td></td>
<td>0.5 mg</td>
<td>1.0 mg</td>
<td>2.0 mg</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Flunisolide 250 mcg/puff</td>
<td>500–750 mcg</td>
<td>1,000–1,250 mcg</td>
<td>NA &gt;1,250 mcg</td>
</tr>
<tr>
<td></td>
<td>500–1,000 mcg</td>
<td>1,250–2,000 mcg</td>
<td>NA &gt;2,000 mcg</td>
</tr>
<tr>
<td>Flunisolide HFA 80 mcg/puff</td>
<td>160 mcg</td>
<td>320 mcg</td>
<td>&gt;320–640 mcg</td>
</tr>
<tr>
<td></td>
<td>320 mcg</td>
<td>&gt;640 mcg</td>
<td>&gt;640 mcg</td>
</tr>
<tr>
<td>Fluticasone HFA/MDI: 44, 110, 220 mcg/puff</td>
<td>88–176 mcg</td>
<td>&gt;176–352 mcg</td>
<td>&gt;352 mcg</td>
</tr>
<tr>
<td></td>
<td>88–264 mcg</td>
<td>352–440 mcg</td>
<td>&gt;440 mcg</td>
</tr>
<tr>
<td>DPI: 50, 100, or 250 mcg/inhalation</td>
<td>100–200 mcg</td>
<td>&gt;200–400 mcg</td>
<td>NA &gt;400 mcg</td>
</tr>
<tr>
<td></td>
<td>100–300 mcg</td>
<td>&gt;400–500 mcg</td>
<td>&gt;500 mcg</td>
</tr>
<tr>
<td>Mometasone DPI 200 mcg/inhalation</td>
<td>200 mcg</td>
<td>400 mcg</td>
<td>NA &gt;400 mcg</td>
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<td>Triamcinolone acetonide 75 mcg/puff</td>
<td>300–600 mcg</td>
<td>&gt;600–900 mcg</td>
<td>NA &gt;900 mcg</td>
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<td>300–750 mcg</td>
<td>900–1,500 mcg</td>
<td>&gt;1,500 mcg</td>
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Key: DPI: dry power inhaler; HFA: hydrofluoroalkane; MDI: metered-dose inhaler; NA: not available (either not approved, no data available, or safety and efficacy not established for this age group)

* Maximum daily dose of budesonide from Symbicort (budesonide/formoterol) is 640 mcg/day, a medium dose of ICS.
Cross References

| Allergy Testing lab01, TRG Medical Policy Manual, Laboratory |
| Cinqair, reslizumab, Medication Policy Manual, Policy No. dru456 |
| Nucala™, mepolizumab, Medication Policy Manual, Policy No. dru428 |

Codes

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References

10. Xolair® (omalizumab) prescribing information, Genentech, Inc; South San Francisco, CA, July 2016.


**Revision History**

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<th>Revision Date</th>
<th>Revision Summary</th>
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<tr>
<td>12/16/2016</td>
<td>Updated the IgE ranges, due to expansion of indications in pediatrics (6 to 12 years of age and down to 20 kg in weight).</td>
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<td>10/21/2016</td>
<td>Update quantity limit.</td>
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<tr>
<td>04/08/2016</td>
<td>No changes.</td>
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