Medication Policy Manual

**Policy No:** dru538

**Topic:** Monoclonal antibodies for asthma and other immune conditions

- benralizumab (Fasenra)
- mepolizumab (Nucala)
- omalizumab (Xolair)
- reslizumab (Cinqair)

**Date of Origin:** April 1, 2018

**Committee Approval Date:** October 23, 2019

**Next Review Date:** January 2020

**Effective Date:** November 15, 2019

**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**

Medications included in this policy are monoclonal antibodies that target specific proteins such as interleukin 5 (IL5) and immunoglobulin E (IgE). They are used to treat several immune diseases such as severe eosinophilic asthma and chronic idiopathic urticaria. Administration is via subcutaneous injection (SC) or intravenous injection (IV).
Policy/Criteria

I. Most contracts require pre-authorization approval of monoclonal antibodies for asthma and other immune conditions prior to coverage. Monoclonal antibodies for asthma and other immune conditions may be considered medically necessary when criteria A, B, or C below are met.

   A. Asthma

   Benralizumab (Fasenra), mepolizumab (Nucala), reslizumab (Cinqair), or omalizumab (Xolair) may be considered medically necessary for severe asthma when there is clinical documentation (including, but not limited to chart notes) that criteria 1. through 7. below are met.

   1. Patient is currently followed by an asthma specialist (allergist, immunologist, or pulmonologist).

   AND

   2. Patient is compliant with maximally tolerated inhaled corticosteroids and long-acting inhaled beta-2 agonist (LABA) therapy (See Appendix 2).

   AND

   3. Patient requires frequent additional medical treatment while on maximally tolerated ICS/LABA therapy. Additional medical treatment could include any of the following within the previous 12 months:

      a. Treatment with two additional courses of oral corticosteroids (e.g. steroid bursts)

      OR

      b. An emergency department (ED) visit or hospitalization.

   AND

   4. There is clinical documentation of limitation of activities of daily living (ADLs), nighttime awakening, or dyspnea.

   AND

   5. An evaluation has been performed to assess for underlying conditions or triggers for asthma or pulmonary disease. If identified, a documented plan is in place to address. Smoking must be discontinued prior to coverage approval.

   AND

   6. [For benralizumab (Fasenra), mepolizumab (Nucala), and reslizumab (Cinqair) only]

   A diagnosis of severe eosinophilic asthma and blood eosinophil count as listed below:

<table>
<thead>
<tr>
<th>Monoclonal Antibody</th>
<th>Blood Eosinophil Count</th>
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<tbody>
<tr>
<td>Benralizumab (Fasenra)</td>
<td>At least 300 cells/microliter</td>
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<tr>
<td>Mepolizumab (Nucala)</td>
<td>At least 150 cells/microliter  OR at least 300 cells/microliter in the past 12 months</td>
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<tr>
<td>Reslizumab (Cinqair)</td>
<td>At least 400 cells/microliter</td>
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AND

7. **[For omalizumab (Xolair) only]**

A diagnosis of severe extrinsic (allergic) asthma and criteria a. and b. below are met:

a. 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

b. Total serum IgE level is one of the following (i. or ii. below):

i. For patients ≥ 12 years of age: 30 to 700 IU/ml

OR

ii. For patients age 6 to <12 years of age, based on weight, as follows in 1. to 7. below:

1. >90 to 150 kg: 30 to 300 IU/ml.
2. >70 to 90 kg: 30 to 500 IU/ml.
3. >60 to 70 kg: 30 to 600 IU/ml.
4. >50 to 60 kg: 30 to 700 IU/ml.
5. >40 to 50 kg: 30 to 900 IU/ml.
6. >30 to 40 kg: 30 to 1,100 IU/ml.
7. 20 to 30 kg: 30 to 1,300 IU/ml.

B. **Chronic Idiopathic/Spontaneous Urticaria (CIU/CSU)**

Omalizumab (Xolair) may be considered medically necessary for CIU/CSU when there is clinical documentation (including, but not limited to chart notes) that criteria 1 through 6 below are met.

1. Patient is currently followed by a specialist (allergist, immunologist, pulmonologist, dermatologist).

AND

2. An evaluation has been performed to rule out other causes of urticaria and identify potential triggers.

AND

3. 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. **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. The patient is compliant with H1 antihistamines (see Appendix 1) at the
maximally tolerated doses, unless contraindicated.

NOTE: Clinical documentation of initial urticaria workup, as well as
subsequent visits, should be submitted for review.

C. Eosinophilic Granulomatosis with Polyangiitis (EGPA, formerly known
as Churg-Strauss Syndrome)

Mepolizumab (Nucala) may be considered medically necessary for EGPA when
there is clinical documentation (including, but not limited to chart notes) that
criteria 1, 2, and 3 below are met.

1. The diagnosis is established by AND the patient is currently being
followed by a specialist (allergist, immunologist, pulmonologist, or
rheumatologist).

AND
2. The patient has a diagnosis of EGPA confirmed by either criteria a. or b.

a. The patient meets four of the six criteria (i. to vi.) below:
   i. History of asthma (wheezing or the finding of diffusion
      high-pitched wheezes in expiration)
   ii. Blood eosinophil count of greater than 10% (% EOS) on
differential white blood count (diff WBC)
   iii. Peripheral neuropathy
   iv. Migratory or transient pulmonary opacities detected
radiographically (such as on chest X-ray; CXR)
   v. Paranasal sinus abnormality
   vi. Blood vessel biopsy (such as artery, arteriole, or venule)
      with extravascular eosinophils

OR
b. The patient meets ALL of the following criteria i. to iii. below:
   i. Medical history of asthma

AND
   ii. Peak blood eosinophil count of greater than 1500
cells/microliter

AND
   iii. Systematic vasculitis involving two or more extra-
pulmonary organs

AND
3. Clinical documentation (including, but not limited to chart notes)
confirming that the patient has a history of EGPA for at least 6 months
with a history of relapsing or refractory disease and criteria a and b are
met.

a. Currently on maximally tolerated oral corticosteroid within the
past 90 days, unless not tolerated or contraindicated.
AND

b. Treatment with an oral DMARD (such as azathioprine or methotrexate) in the past 90 days has been ineffective, not tolerated, or all oral DMARDs are contraindicated.

II. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services considers benralizumab (Fasenra) [prefilled autoinjector] and mepolizumab (Nucala) [prefilled autoinjector] to be a self-administered medications.

B. Regence Pharmacy Services does not consider benralizumab (Fasenra) [prefilled syringe], mepolizumab (Nucala) [vial], omalizumab (Xolair) [vial AND prefilled syringe], and reslizumab (Cinqair) to be self-administered medications.

C. When pre-authorization is approved, each drug may be covered in the following quantities and for the following authorization periods outlined in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Authorization Limits</th>
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<td><strong>Benralizumab</strong> (Fasenra)</td>
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<td><strong>Mepolizumab</strong> (Nucala)</td>
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### Table 1. Authorization Limits

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<th>Medication</th>
<th>Condition</th>
<th>Limitation</th>
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| Omalizumab       | Severe extrinsic (allergic) asthma       | - Up to 375 mg (up to three - single-dose 150 mg vials [total of 3 mL] OR two - 150 mg and one - 75 mg single-dose prefilled syringes [total of 2.5 mL]) every 14 days.  
- Authorization may be initially authorized for 6 months. After the initial authorization, coverage may be reviewed at least every 12 months to confirm that current medical necessity criteria are met and that the medication is effective defined as sustained clinical improvement from reduced asthma/ symptoms (such as reduced missed days from work or school) or stable asthma control. |
| Idiopathic urticaria: | - Up to 300 mg (two - 150 mg single-dose vials OR two – 150 mg prefilled syringes) every 28 days.  
- Authorization may be initially authorized for 6 months. After the initial authorization, coverage may be reviewed at least every 12 months to confirm that current medical necessity criteria are met and that the medication is effective defined as sustained clinical improvement from reduced urticaria symptoms (such as reduced missed days from work or school) or stable asthma control. |
| Reslizumab       | Severe eosinophilic asthma               | Up to 3 mg/kg every 28 days.  
- Authorization may be initially authorized for 6 months. After the initial authorization, coverage 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 symptoms (such as reduced missed days from work or school) or stable asthma control. |

### III. Not Medically Necessary Uses

A. Omalizumab (Xolair) is considered not medically necessary when used for allergic rhinitis.

### IV. Investigational Uses

A. Combination use of any monoclonal antibodies in this policy.

B. Sequential use of anti-IL5 monoclonal antibodies, for any indication

C. Dose escalations in excess of those listed in Section II, Table 1 (above) is considered investigational for any indication.

D. Unless otherwise specified in Section I, medications included in this policy are considered investigational when used for all other conditions, due to lack of published data, lack of high quality data, or lack of positive data. Details of select investigational uses are listed below.
Allergic bronchopulmonary aspergillosis (ABPA)
- There is insufficient evidence to establish the efficacy of monoclonal anti-IgE or anti-IL5 antibodies for the treatment of ABPA.
- The one small crossover trial (n=13) found a reduction in exacerbations over a 4-month period in ABPA patients with use of high-dose omalizumab (Xolair) (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 (Xolair) for ABPA. [1]

Atopic dermatitis
- There is insufficient evidence to support the use of monoclonal anti-IgE or anti-IL5 antibodies for atopic dermatitis.[2,3]
- Mepolizumab (Nucala) has been studied in atopic dermatitis, and no significant benefit was observed.

Chronic obstructive pulmonary disease (COPD)
- There is no reliable evidence to establish efficacy or safety of monoclonal anti-IgE or anti-IL5 antibodies for the treatment of eosinophilic COPD.
- Mepolizumab (Nucala) was studied in two phase 3 trials evaluating annual COPD exacerbation rate; however, the benefit with mepolizumab (Nucala) was not consistently demonstrated in patients with eosinophilic COPD. Despite promising results of clinical trials, high quality, long-term clinical trials are needed to confirm efficacy and safety of mepolizumab (Nucala) in this setting. [4]
- Additional studies are ongoing for benralizumab (Fasenra).

Eosinophilic esophagitis (EE)
- There is no reliable evidence to establish efficacy or safety of monoclonal anti-IgE or anti-IL5 antibodies in the treatment of eosinophilic esophagitis.
- One small trial found no benefit of omalizumab (Xolair) in patients with eosinophilic esophagitis. [5]

Eosinophilic granulomatosis with polyangiitis (EGPA) / allergic granulomatosis / Churg-Strauss syndrome
- There are no published clinical trials evaluating the safety or efficacy of omalizumab (Xolair), benralizumab (Fasenra), and reslizumab (Cinqair) for the treatment of EGPA. Additional studies are ongoing for benralizumab (Fasenra) and reslizumab (Cinqair). [6]
**Hypereosinophilic syndrome (HES, “hyper-E”)**

- There is insufficient evidence to support the use of monoclonal anti-IgE or anti-IL5 antibodies for hypereosinophilic syndrome.
- The safety and effectiveness of mepolizumab (Nucala) in hypereosinophilic syndrome, have not been established. Although initial results are promising, the evidence is limited to Phase 2 trials and one open-label Phase 3 trial in HES (an extension from a Phase 2 trial). Additional studies are ongoing. \(^{[7,8]}\)

**Chronic rhinosinusitis with Nasal polyposis (CRSwNP)**

- There is insufficient evidence to establish the safety and efficacy of monoclonal anti-IgE or anti-IL5 antibodies for the treatment of nasal polyposis. Additional trials are ongoing for mepolizumab (Nucala). \(^{[9]}\) See dupilumab (Dupixent) policy for details on coverage for CRSwNP.

**Peanut or other food allergies**

- There is insufficient evidence to establish the efficacy of monoclonal anti-IgE and anti-IL5 antibodies for the treatment of food allergies.
- Phase 2 results suggest benefits of another anti-IgE compound-TNX-901 for treatment of peanut allergy, which cannot be extrapolated to the use of omalizumab (Xolair) to protect against anaphylaxis in patients with peanut allergy. \(^{[10]}\)

**Urticaria, non-idiopathic (e.g. cold-induced)**

- There is insufficient evidence to support the use of omalizumab (Xolair) for the treatment of non-idiopathic urticaria, such as cold-induced urticaria. The evidence is limited to case reports. \(^{[11]}\)

**Position Statement**

**Summary**

- Monoclonal anti-IgE and anti-IL5 antibodies may be covered for specific diagnoses where there is demonstrated safety and efficacy from randomized, controlled trials to support their use, including asthma and other specific indications.
  
  * Anti-IgE monoclonal antibodies [e.g. omalizumab (Xolair)] reduces the levels of circulating immunoglobulin E (IgE) and inhibits binding of IgE to mast cells, to prevent the activation of the allergic cascade and decrease inflammation.
  
  * Anti-IL5 antibodies [e.g. benralizumab (Fasenra), mepolizumab (Nucala), and reslizumab (Cinqair)] prevent activation of interleukin 5 (IL-5) that is responsible for the growth and survival of eosinophils, to decrease inflammation.
  
  * Interleukin-4 receptor antagonist [dupilumab (Dupixent)] is also used for add-on maintenance treatment for asthma (covered in a separate policy; see Cross References).
**Asthma**

* Monoclonal respiratory antibodies may be coverable for poorly controlled asthma, despite use of maximal step therapy, which includes patient compliance with therapy and an assessment for triggers, as well as a plan to control identified triggers.

* The monoclonal respiratory antibodies can target IgE (Xolair) or eosinophils (Cinqair, Fasenra, and Nucala). They may be covered when there is documentation of either IgE or eosinophils elevation, according to the levels studied in clinical trials and found to be beneficial. Use of monoclonal respiratory antibodies for management of IgE or eosinophil levels outside of these ranges is not coverable.

* For severe asthma (STEP 5), Global Initiative for Asthma (GINA) guidelines recommend high-dose ICS- inhaled long-acting beta-agonist (LABA) therapy. As needed low dose ICS-formoterol is recommended for immediate relief of symptoms. Add-on therapy with a biologic agent or tiotropium may be considered after phenotypic assessment. [12]

  - In patients with severe eosinophilic asthma uncontrolled on STEP 4-5 treatment, mepolizumab (Nucala), reslizumab (Cinqair), or benralizumab (Fasenra) are recommended as add-on treatment options. [13]

  - In patients with IgE-mediated allergic asthma uncontrolled on STEP 5 treatment, omalizumab (Xolair) is recommended as add-on therapy. [13]

* Monoclonal anti-IgE and anti-IL5 antibodies have not been proven to be safer or more effective than step therapy options recommended in treatment guidelines, nor in patients with less severe asthma, noneosinophilic asthma, or non-allergic asthma. [14]

* There is insufficient evidence that any one monoclonal antibody for uncontrolled asthma is superior to another. There are no comparative trials. Based on indirect trial comparisons, the benefits are roughly equivalent (rate of exacerbations).

**Chronic Idiopathic/Spontaneous Urticaria (CIU/CSU) (Xolair)**

* Omalizumab (Xolair) may be coverable for poorly controlled chronic idiopathic urticaria despite use of maximal step therapy, which includes patient compliance with antihistamines and an assessment for other causes, including triggers, as well as a plan to control identified triggers.

* Standard of care for chronic urticaria includes identification and elimination of the underlying aggravating triggers followed by use of antihistamines. [15]

* Other potential therapies include leukotriene antagonists (such as montelukast), cyclosporine, dapsone, other oral DMARDs, and corticosteroids.

* All patients in clinical trials of omalizumab (Xolair) for urticaria were refractory to antihistamines.

* Omalizumab (Xolair) may have some impact on severe, chronic refractory idiopathic urticaria; however, the clinical benefit is uncertain. 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.
• Omalizumab (Xolair) has not been proven to be safer or more effective than step therapy options recommended in treatment guidelines, nor in patients with less severe urticaria.

Eosinophilic granulomatosis with polyangiitis (EGPA) (Nucala)

* Mepolizumab (Nucala) may be coverable for relapsing or refractory EGPA when specific diagnostic criteria for EGPA are met and persistent disease despite use of maximal step therapy, which includes steroids and immunosuppressants (oral DMARDs).

* Glucocorticoids are the mainstay of therapy for EGPA. [16,17] Patients in clinical trials of mepolizumab (Nucala) for EGPA were relapsing or refractory to corticosteroids with or without immunosuppressives.

* Immunosuppressive oral DMARD therapy [e.g. azathioprine, methotrexate] is used as add-on therapy for patients with life and/or organ manifestations for maintenance of remission.

* Other second line therapy options for EGPA include rituximab, immunoglobulins, and interferon-alpha.

Monoclonal respiratory antibodies may be covered at the doses proven to be safe and effective for asthma and other associated conditions in clinical trials (as detailed in Section II above). The safety and effectiveness of higher doses for monoclonal anti-IgE and anti-IL5 antibodies have not been established. the dose proven to be safe and effective for management of refractory eosinophilic asthma.

Monoclonal anti-IgE and anti-IL5 antibodies, with the exception of mepolizumab autoinjector (Nucala), are not considered self-administered medications and must be administered by a health care provider. Although omalizumab (Xolair) is now available in a single-dose pre-filled syringe, it is not labeled for self-administration and is only coverable as a provider-administered medication.

Omalizumab (Xolair) 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.

The safety and efficacy of monoclonal anti-IgE and anti-IL5 antibodies in combination with other anti-asthma monoclonal antibodies or in conditions not included in coverage criteria (as listed in Section I.) have not been established. There are no trials of the use of anti-asthma monoclonal antibodies as combination or sequential therapy. Additional trials are ongoing.
Clinical Efficacy

ASTHMA BACKGROUND

- 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). Eosinophilic asthma is a sub phenotype of severe asthma characterized by elevated sputum and blood eosinophil levels as well as increased asthma severity, atopy, late-onset disease, and steroid refractoriness.

- IgE may be in the inflammatory cascade of some events leading to asthmatic airway inflammation. Anti-IgE monoclonal antibody, omalizumab (Xolair) binds circulating IgE.

- Anti-IL5 monoclonal antibodies (Cinqair, Nucala, and Fasenra) specifically target formation of eosinophils and depletes blood eosinophil levels.

* Various peripheral blood eosinophil levels were studied in clinical trials.

* The eosinophil levels in the coverage criteria are based on the efficacy data from the clinical trials of these medications and where they were found to be most effective. Global Initiative for Asthma (GINA) guidelines recommend STEP 5 add-on therapy with long acting muscarinic antagonists (LAMA) such as tiotropium, anti-IgE therapy (omalizumab), anti-interleukin-5 therapy, or anti-interleukin-4 therapy after phenotypic assessment of asthma subtype. [18]

- There is no reliable evidence to establish efficacy or safety of monoclonal anti-IL5 antibodies for severe allergic asthma without documentation of severe eosinophilia. [3]

Benralizumab (Fasenra) for Eosinophilic Asthma

- Two randomized, double-blinded, placebo-controlled studies (SIROCCO and CALIMA) evaluated the safety and efficacy of benralizumab (Fasenra) 30 mg in patients with severe eosinophilic asthma, uncontrolled on moderate- to high-doses ICS. [19,20]

* The trials enrolled patients with a history of two or more asthma exacerbations requiring oral or systemic corticosteroid treatment in the past 12 months despite medium to high dose ICS/LABA. Patients were stratified by baseline blood eosinophil count (≤ 300 or ≥ 300 cells/microliter).

* The primary endpoint was reduction in asthma exacerbations for patients with baseline blood eosinophil count ≥ 300 cells/microliter in both studies. After 48-56 weeks, benralizumab (Fasenra) reduced the annual rate of exacerbations by 28-51% compared to placebo.

* However, in the SIROCCO trial, only patients with a baseline blood eosinophil count ≥ 300 cells/microliter responded to the standard starting dose of benralizumab (Fasenra) 30 mg every 8 weeks. For patients with baseline blood eosinophil count < 300 cells/microliter, response was seen only with double the dose (30 mg every 4 weeks).

- In CALIMA, patients on medium-dose ICS/LABA were included. Therefore, the generalizability of the results to patients optimized on standard STEP 5 therapy with high-dose ICS/LABA is uncertain. One double-blind, multicenter, randomized study evaluated the efficacy of benralizumab (Fasenra) on oral corticosteroid (OCS) reduction compared to placebo. [21]
Patients were required to have a daily oral corticosteroid dose between 7.5 to 40 mg per day in addition to high dose ICS/LABA and a baseline eosinophil count of at least 150 cells/microliter.

Patients in the benralizumab (Fasenra) arms (30 mg every q 4 weeks or every 8 weeks) had a statistically significant reduction in daily OCS compared to placebo (75% vs. 25%, respectively). However, the external validity of the results is uncertain, given the inclusion of patients on medium-dose ICS/LABA.

The role of benralizumab (Fasenra) for patients with a baseline blood eosinophil count of < 300 cells/microliter is unclear. The overall assessment of benefit is uncertain, with inconsistent response to standard starting dosing and confounded baseline characteristics. Patients in two of the three trials were not on optimized high-dose ICS/LABA, as is the standard STEP5 (NHLBI and GINA guidance), prior to addition of anti-IL5 therapy.

In the SIROCCO trial, patients were optimized on high dose ICS/LABA. However, there was no statistical reduction in the rate of asthma exacerbations for patients with baseline blood eosinophil count of < 300 in the arm of benralizumab (Fasenra) 30 mg every 8 weeks. Benefit was seen only at higher dosing (30 mg every 4 weeks). As such, benralizumab (Fasenra) if coverable only for patients with baseline blood eosinophil count of ≥ 300 cells/microliter.

In the CALIMA and ZONDA trials, there was statistically significant response to standard benralizumab (Fasenra) 30 mg every 8 weeks. However, patients were NOT optimized on high-dose ICS/LABA prior to enrollment. Both studies included patients on medium dose ICS/LABA, which is not reflective of Step 5 of NHLBI Guidelines for add-on IL-5 therapy. Therefore, the benefit in optimized Step 5 asthma patients with an eosinophil count of <300 is unknown.

- In CALIMA, there was a statistically significant reduction in asthma exacerbation rates for patients with baseline blood eosinophil count of < 300 cells/microliter in the arm of benralizumab (Fasenra) 30 mg every 8 weeks; however, because baseline ICS/LABA was not maximized, the external validity of this finding for use in a STEP5 therapy optimized patient is unknown. [Fitzgerald, PMID 27609406]

- In ZONDA, there was a statistically significant reduction in the need for oral steroids for patients with baseline blood eosinophil count of >150 cells/microliter with benralizumab (Fasenra); however, because baseline ICS/LABA was not maximized, the external validity of this finding for use in a STEP 5 therapy optimized patient is unknown. [Nair, PMID 28530840]

Because the benefit of benralizumab (Fasenra) in STEP 5 therapy optimized patients with a baseline eosinophil count of <300 is unclear and there are other coverable treatment options for patients with an eosinophil count of 150 to 300 (see Section I), the use of benralizumab (Fasenra) in patients with a baseline eosinophil count of <300 cannot be covered.
Mepolizumab (Nucala) for Eosinophilic Asthma

- One randomized, double-blinded, placebo- and active-controlled, 32-week study evaluated the safety and efficacy of mepolizumab (Nucala) 75 mg or 100 mg compared to placebo in patients with severe refractory eosinophilic asthma. [22]

* The trial enrolled patients with blood eosinophil counts ≥ 150 cells/microliter within 6 weeks of dosing or ≥ 300 cells/microliter within 12 months.

* The primary endpoint was frequency of asthma exacerbations. Mepolizumab (Nucala) demonstrated a statistically significant reduction of annual exacerbation rates by 13% compared to placebo.

- One randomized, controlled trial evaluated the efficacy of mepolizumab (Nucala) in reducing daily oral corticosteroid dose compared to placebo. [23]

* The primary end point was percent reduction of oral corticosteroid dose during weeks 20 to 24 without loss of asthma control. Overall, mepolizumab (Nucala) achieved greater reduction in oral corticosteroid use while maintaining asthma control when compared to placebo. However, the difference between the mepolizumab (Nucala) and placebo groups was not statistically significant.

- Mepolizumab (Nucala) has been studied in moderate persistent asthma, and no significant benefit was observed. [24]

Omalizumab (Xolair) for Extrinsic (allergic) Asthma

- One high quality meta-analysis evaluated the efficacy of omalizumab (Xolair) in reducing asthma exacerbations and corticosteroid use compared to placebo.

* After 16 to 60 weeks, omalizumab (Xolair) reduced asthma exacerbations from 26% to 16% of patients suffering from an exacerbation.

* An absolute reduction in hospitalization risk was reduced from 3% to 0.5% with omalizumab (Xolair) over 28 to 60 weeks.

- Omalizumab (Xolair) increases the number of asthma patients who are able to reduce or withdraw their inhaled steroids and is effective in reducing asthma. [25-28]

- There is no available data demonstrating that omalizumab (Xolair) is superior to step therapy options (e.g. ICS/LABAs and oral steroids for exacerbations) recommended in treatment guidelines for moderate-to-severe persistent asthma.

- Optimal clinical response to omalizumab (Xolair) 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 (Xolair) 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 (Xolair) clinical trials). [29]

- 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. [30]
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 in adults. There is no established dose or benefit for IgE levels outside of this range.
- Efficacy and dosing of omalizumab (Xolair) in asthma patients (> 50 kg) with IgE levels less than 30 or greater than 700 have not been established. 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 (Xolair) in patients age 6 to less than 12 years old with a baseline IgE as follows:
  * >90 to 150 kg: baseline IgE of 30 to 300 IU/ml
  * >70 to 90 kg: baseline IgE of 30 to 500 IU/ml
  * >60 to 70 kg: baseline IgE of 30 to 600 IU/ml
  * >50 to 60 kg: baseline IgE of 30 to 700 IU/ml
  * >40 to 50 kg: baseline IgE of 30 to 900 IU/ml
  * >30 to 40 kg: baseline IgE of 30 to 1,100 IU/ml
  * 20 to 30 kg: baseline IgE of 30 to 1,300 IU/ml
As with adults, there is no established dose or benefit for IgE levels outside of this range.

- Monitoring IgE levels after administration of omalizumab (Xolair) are problematic, as IgE levels post-administration measure both bound and unbound (free) IgE.

Reslizumab (Cinqair) for Eosinophilic Asthma

- Reslizumab (Cinqair) has been studied in people with moderate and severe refractory eosinophilic asthma that is inadequately controlled despite use of high-dose corticosteroids and a controller medication.
- Two double-blind, controlled studies evaluated the efficacy of reslizumab (Cinqair) 3 mg/kg compared to placebo in patients with severe eosinophilic asthma.
  * Patients were required to have at least 1 asthma exacerbation requiring systematic corticosteroids.
  * The primary endpoint was frequency of asthma exacerbation. After 52 weeks, reslizumab (Cinqair) reduced the annual asthma exacerbation rate by 10-14% compared to placebo.

CHRONIC IDIOPATHIC URTICARIA (CIU/CSU) BACKGROUND

- 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.
- 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.
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. However, in clinical trials, all patients had CIU symptoms for at least 6 months. 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.

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. Primary treatment for CU should include aggravating trigger control and histamine blockade. Refractory patients may be responsive to omalizumab (Xolair).

Omalizumab (Xolair) for CIU/CSU

Two randomized, double-blinded, placebo-controlled 12- to 24-week studies evaluated the safety and efficacy of omalizumab (Xolair) in patients with refractory chronic idiopathic/spontaneous urticaria. The trial enrolled patients with a urticaria activity score (UAS) > 4 despite use of H1-antihistamines and a weekly itch severity score (ISS) > 8. The primary endpoint of the study was change from baseline in weekly ISS at week 12. Additional endpoints included the change in UAS over 7 days and proportion of complete responders. Mean change in weekly ISS with omalizumab (Xolair) decreased by -3.0 from placebo. Although, this is a subjective endpoint with a lack of defined minimal clinically important difference, it is clinically relevant to patients. The FDA recognizes reduction of itching as the most important outcome.

Omalizumab (Xolair) 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 (Xolair) has not been proven to eliminate itching or improve functional impairment due to urticaria symptoms. Patients with a clearly defined cause for urticaria, such as physical cause, were excluded from clinical trials. Omalizumab (Xolair) has only been studied as add-on therapy. All patients in clinical trials of omalizumab (Xolair) for chronic urticaria were refractory to antihistamines. However, omalizumab (Xolair) has not been compared to the many other available therapies for antihistamine-refractory urticaria. Therefore, it is unknown if omalizumab (Xolair) is superior to these less-costly alternatives.
- IgE levels are not measured nor used as a marker for omalizumab (Xolair) therapy with urticaria.

EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA) BACKGROUND

- Eosinophilic granulomatosis with polyangiitis, also known as allergic granulomatosis or Churg-Strauss syndrome, is a multisystem autoimmune syndrome characterized by eosinophil-rich granulomatosis inflammation of microscopic vessels. The respiratory tract is typically affected, and EGPA commonly includes asthma among its manifestations; however, widespread manifestations are found, including neurological, cardiac, and renal involvement.

- Classification of EGPA is most often according to 1990 classification criteria from the American College of Rheumatology. Patients with vasculitis may be classified as having EGPA if they have at least 4 of 6 typical findings: [41]
  * Asthma (a history of wheezing or finding or diffuse high pitched wheezes on expiration)
  * Greater than 10 percent eosinophils on the differential leukocyte count
  * Mononeuropathy (including multiplex) or polyneuropathy
  * Migratory or transient opacities detected radiographically
  * Paranasal sinus abnormality
  * Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas

- The primary therapy for EGPA is systemic corticosteroids. An additional immunosuppressive agent (e.g. cyclophosphamide) is typically added for patients with more advanced or refractory disease and in those whose disease flares with tapering of systemic glucocorticoids. Once remission is induced, patients are switched to less toxic immunosuppressives, such as azathioprine or methotrexate, for maintenance therapy. Second or third-line drugs include rituximab, immunoglobulins, and interferon-alpha. [16,17]

Mepolizumab (Nucala) for EGPA

- The MIRRA trial (multicenter, randomized, double-blind, controlled) evaluated the efficacy of mepolizumab (Nucala) 300 mg in patients with relapsing or refractory EGPA not optimally controlled with an oral corticosteroid with or without oral DMARDs compared to placebo. [6]
  * The primary endpoint was total accrued weeks of remission. Mepolizumab (Nucala) was found to result in significantly more weeks in remission than placebo (28% vs. 3% of patients had ≥ 24 weeks of accrued remission).
  * After 48 weeks, 32% of mepolizumab (Nucala) patients remained in remission allowing for reduced corticosteroid use compared to 3% of placebo patients.

- Mepolizumab (Nucala) has only been studied as add-on therapy for EGPA. It has not been compared to oral DMARDs for corticosteroid-refractory EGPA. Therefore, it is unknown if mepolizumab (Nucala) is superior to these less-costly alternatives.
**Not Medically Necessary Uses**

- Omalizumab (Xolair) reduces seasonal and perennial allergic rhinitis symptoms, but has not been shown to have better efficacy than first-line alternatives, such as nasal corticosteroids, antihistamines, or allergen desensitization therapy. [42-44]

**Safety**

- All monoclonal antibodies for asthma have a theoretical risk of opportunistic infections (including parasitic infections) and malignancy. Immunogenicity and development of antidrug antibodies was observed in clinical trials of mepolizumab (Nucala) and reslizumab (Cinqair).

- Anaphylaxis is a concern with administration of anti-asthma monoclonal antibodies. Omalizumab (Xolair) and reslizumab (Cinqair) have a boxed warning for anaphylaxis.

  * Benralizumab (Fasenra), omalizumab (Xolair), and reslizumab (Cinqair) are administered only by a health care professional, who can monitor for and treat anaphylactic reactions. [30,45,46]

  * Mepolizumab (Nucala) is the only asthma monoclonal antibody that is labeled for patient self-administration, once a provider determines self-administration is appropriate. [47]

- FDA long-term safety data suggests a slightly elevated risk of cardiovascular and cerebrovascular adverse events with omalizumab (Xolair). [30]

- The recommended dosing and administration for monoclonal anti-IgE and IL5 antibodies are listed in Table 2 below.

- The safety and effectiveness of dose escalation for patients not responding to these standard doses have not been established.
### Table 2: Recommended Dosing and Administration for Monoclonal anti-IgE and anti-IL5 Antibodies

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benralizumab (Fasenra) [46]</td>
<td>- Severe eosinophilic asthma: 30 mg subcutaneously once every 4 weeks for the first three doses, then once every 8 weeks thereafter.</td>
</tr>
</tbody>
</table>
| Mepolizumab (Nucala)  [47] | - Severe eosinophilic asthma: 100 mg subcutaneously once every 4 weeks.  
- EGPA: 300 mg (3 separate 100-mg injections) subcutaneously once every 4 weeks.                                                                                                                                                                                                    |
| Omalizumab (Xolair) [30] | - Asthma: 75 to 375 mg subcutaneously once every 2 or 4 weeks.  
- Determine dose and dosing frequency by serum total IgE level (IU/mL) measured before the start of treatment, and by body weight.  
- Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during omalizumab (Xolair) treatment cannot be used as a guide for dose determination.  
- Chronic idiopathic urticaria: 150 or 300 mg subcutaneously once every 4 weeks.  
- Dosing of omalizumab (Xolair) in CIU patients is not dependent on serum IgE (free or total) level or body weight.                                                                                                                                                                  |
| Reslizumab (Cinqair) [45] | - Severe eosinophilic asthma: 3 mg/kg intravenously once every 4 weeks over 20-50 minutes.  
- Reslizumab (Cinqair) is for intravenous infusion over. Do not administer as an intravenous push or bolus.                                                                                                                                                                                         |
# Appendix 1: Antihistamines

## H₁-Antihistamines

*First Generation (non-selective, “sedating”)*
- brompheniramine
- chlorpheniramine (generic Chlor-Trimeton)
- clemastine (generic Tavist)
- cyproheptadine (generic Periactin)
- dexbrompheniramine
- dexchlorpheniramine
- 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)

## H₂-Antihistamines
- cimetidine (generic Tagamet)
- famotidine (generic Pepcid)
- nizatidine (generic Aclid)
- ranitidine (generic Zantac)
Appendix 2: Low, Medium, and High Daily Doses of Inhaled Corticosteroids (Adapted from GINA 2019 Guidelines)[13]

### Adults and Adolescents (Age 12 years and Older)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Products</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone dipropionate (CFC)</td>
<td>None</td>
<td>200-500</td>
<td>&gt;500-1000</td>
<td>&gt;1000</td>
</tr>
<tr>
<td>Beclomethasone dipropionate (HFA)</td>
<td>QVAR Redihaler</td>
<td>100-200</td>
<td>&gt;200-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Budesonide (DPI)</td>
<td>Symbicort, Pulmicort Flexhaler</td>
<td>200-400</td>
<td>&gt;400-800</td>
<td>&gt;800</td>
</tr>
<tr>
<td>Ciclesonide (HFA)</td>
<td>Alvesco</td>
<td>80-160</td>
<td>&gt;160-320</td>
<td>&gt;320</td>
</tr>
<tr>
<td>Fluticasone furoate (DPI)</td>
<td>Breo Ellipta, Arnuity Ellipta, Trelegy Ellipta</td>
<td>100</td>
<td>N/A</td>
<td>200</td>
</tr>
<tr>
<td>Fluticasone propionate (DPI)</td>
<td>Advair Diskus, Flovent Diskus, Wixela Inhub, AirDuo RespiClick, ArmonAir RespiClick</td>
<td>100-250</td>
<td>&gt;250-500</td>
<td>&gt;500</td>
</tr>
<tr>
<td>Fluticasone propionate (HFA)</td>
<td>Advair HFA, Flovent HFA</td>
<td>100-250</td>
<td>&gt;250-500</td>
<td>&gt;500</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Dulera, Asmanex</td>
<td>110-220</td>
<td>&gt;220-440</td>
<td>&gt;440</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Azmacort</td>
<td>400-1000</td>
<td>&gt;1000-2000</td>
<td>&gt;2000</td>
</tr>
</tbody>
</table>

Key: DPI: dry power inhaler; HFA: hydrofluoroalkane;

### Children age 6-11 years

<table>
<thead>
<tr>
<th>Drug</th>
<th>Products</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone dipropionate (CFC)</td>
<td>None</td>
<td>100-200</td>
<td>&gt;200-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Beclomethasone dipropionate (HFA)</td>
<td>QVAR Redihaler</td>
<td>50-100</td>
<td>&gt;100-200</td>
<td>&gt;200</td>
</tr>
<tr>
<td>Budesonide (DPI)</td>
<td>Symbicort, Pulmicort Flexhaler</td>
<td>100-200</td>
<td>&gt;200-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Ciclesonide (HFA)</td>
<td>Alvesco</td>
<td>80</td>
<td>&gt;80-160</td>
<td>&gt;160</td>
</tr>
<tr>
<td>Fluticasone furoate (DPI)</td>
<td>Breo Ellipta, Arnuity Ellipta, Trelegy Ellipta</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Fluticasone propionate (DPI)</td>
<td>Advair Diskus, Flovent Diskus, Wixela Inhub, AirDuo RespiClick, ArmonAir RespiClick</td>
<td>100-200</td>
<td>&gt;200-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Fluticasone propionate (HFA)</td>
<td>Advair HFA, Flovent HFA</td>
<td>100-200</td>
<td>&gt;200-500</td>
<td>&gt;500</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Dulera, Asmanex</td>
<td>110</td>
<td>≥220-&lt;440</td>
<td>≥440</td>
</tr>
<tr>
<td>Drug</td>
<td>Products</td>
<td>Daily Dose</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
<td>------------</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>Beclomethasone dipropionate (HFA)</td>
<td>QVAR RediHaler</td>
<td>100 (ages ≥5 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide nebulized</td>
<td>Generic</td>
<td>500 (ages ≥1 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide pressurized MDI</td>
<td>Pulmicort Flexhaler</td>
<td>Not sufficiently studied in this age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclesonide (HFA)</td>
<td>Alvesco</td>
<td>Not sufficiently studied in this age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone propionate (HFA)</td>
<td>Flovent HFA</td>
<td>50 (ages ≥4 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Asmanex</td>
<td>110 (ages ≥4 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Azmacort</td>
<td>Not sufficiently studied in this age group</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key: DPI: dry power inhaler; HFA: hydrofluoroalkane;

### Appendix 3: Inhaled Corticosteroid/Long-acting Beta-agonist (ICS/LABA) Combinations

<table>
<thead>
<tr>
<th>Product</th>
<th>Dosing</th>
<th>Max puff/day</th>
<th>High Dose?</th>
<th>Available strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluticasone propionate / salmeterol DPI (Advair Diskus)</td>
<td>Twice daily</td>
<td>2 (1,000 mcg)</td>
<td>Yes (≥500)</td>
<td>100/50, 250/50, 500/50</td>
</tr>
<tr>
<td>fluticasone propionate/ salmeterol MDI (Advair HFA)</td>
<td>Twice daily</td>
<td>4 (920 mcg)</td>
<td>Yes (≥440)</td>
<td>45/21, 115/21, 230/21</td>
</tr>
<tr>
<td>budesonide + formoterol MDI (Symbicort)</td>
<td>Twice daily</td>
<td>4 (640 mcg)</td>
<td>No</td>
<td>80/4,5, 160/4,5</td>
</tr>
<tr>
<td>fluticasone propionate / salmeterol DPI (AirDuo RespiClick)</td>
<td>Twice daily</td>
<td>2 (464 mcg)</td>
<td>No</td>
<td>55/14, 113/14, 232/14</td>
</tr>
<tr>
<td>mometasone/ formoterol MDI (Dulera)</td>
<td>Twice daily</td>
<td>4 (800 mcg)</td>
<td>Yes (≥400)</td>
<td>100/5, 200/5</td>
</tr>
<tr>
<td>fluticasone furoate/vilanterol DPI (Breo Ellipta)</td>
<td>Once daily</td>
<td>1 (200 mcg)</td>
<td>Yes (≥200)</td>
<td>100/25, 200/25</td>
</tr>
</tbody>
</table>

*a* High dose budesonide is >1,200 mcg/day. Maximum daily dose of budesonide from Symbicort (budesonide/formoterol) is 640 mcg/day, a medium dose of ICS.

*b* High dose fluticasone propionate DPI is >500 mcg/day. Maximum daily dose of fluticasone propionate from AirDuo RespiClick (fluticasone propionate/salmeterol DPI) is 464 mcg/day, a medium dose of ICS.
Cross References

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Lab01, TRG Medical</td>
<td>Allergy Testing Laboratory</td>
</tr>
<tr>
<td>Policy Manual</td>
<td>Non-Preferred Inhaled Corticosteroid-Containing Medications Policy No. dru380</td>
</tr>
<tr>
<td>Medication Policy</td>
<td>Dupixent, dupilumab Medication Policy Manual Policy No. dru493</td>
</tr>
<tr>
<td>Manual, Laboratory</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td>J2182</td>
<td>Injection, mepolizumab, 1 mg</td>
</tr>
<tr>
<td>HCPCS</td>
<td>J2357</td>
<td>Injection, omalizumab, 5 mg</td>
</tr>
<tr>
<td>HCPCS</td>
<td>J2786</td>
<td>Injection, reslizumab, 1 mg</td>
</tr>
</tbody>
</table>

References


45. Cinqair (reslizumab) [prescribing information]. Frazer, PA: Teva; March 2016.
46. Fasenra [prescribing information]. Wilmington, DE: AstraZeneca; 11/2017

Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/23/2019</td>
<td>- Added benralizumab (Fasenra) and mepolizumab (Nucala) single-dose pre-filled autoinjector for self-administration to the policy. All other anti-asthma antibodies in the policy remain provider-administered only. Effective November 15, 2019.</td>
</tr>
<tr>
<td></td>
<td>- Updated coverage criteria for asthma:</td>
</tr>
<tr>
<td></td>
<td>▪ Clarified that maximally tolerated inhaled corticosteroid and long-acting inhaled beta-2 agonist therapy must have been tried.</td>
</tr>
<tr>
<td></td>
<td>▪ Removed requirement for use of oral corticosteroids, if exacerbations are present.</td>
</tr>
<tr>
<td></td>
<td>▪ Revised definition of poor asthma control to include clarify requirement for two additional oral corticosteroid bursts or emergency department visits or hospitalizations.</td>
</tr>
<tr>
<td>4/25/2019</td>
<td>Updated and fixed incorrect references. No changes to policy criteria with this update.</td>
</tr>
<tr>
<td>1/31/2019</td>
<td>Clarified intent of trigger criteria.</td>
</tr>
<tr>
<td>11/16/2018</td>
<td>Clarified intent of trigger, step therapy, quantity limit and reauthorization criteria.</td>
</tr>
<tr>
<td>03/16/2018</td>
<td>New policy:</td>
</tr>
<tr>
<td></td>
<td>- The Xolair, Nucala, and Cinqair policies were combined.</td>
</tr>
<tr>
<td></td>
<td>- Coverage criteria added for asthma for newly-approved Fasenra.</td>
</tr>
<tr>
<td></td>
<td>- Coverage criteria added for EGPA for Nucala.</td>
</tr>
</tbody>
</table>

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