

RESPIRATORY INTERLEUKINS (CINQAIR®, FASENRA®, AND NUCALA®)

Policy Number: PHARMACY 293.7 T2

Effective Date: January 1, 2019

| Table of Contents | Page |
|---|-------------|
| INSTRUCTIONS FOR USE | 1 |
| CONDITIONS OF COVERAGE | 1 |
| BENEFIT CONSIDERATIONS | 2 |
| COVERAGE RATIONALE | 2 |
| U.S. FOOD AND DRUG ADMINISTRATION | 6 |
| BACKGROUND | 6 |
| APPLICABLE CODES | 7 |
| CLINICAL EVIDENCE | 7 |
| REFERENCES | 8 |
| POLICY HISTORY/REVISION INFORMATION | 9 |

Related Policy

- [Acquired Rare Disease Drug Therapy Exception Process](#)

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

CONDITIONS OF COVERAGE

| | |
|--|---|
| Applicable Lines of Business/Products | This policy applies to Oxford Commercial plan membership. |
| Benefit Type | General Benefits Package |
| Referral Required (Does not apply to non-gatekeeper products) | No |
| Authorization Required (Precertification always required for inpatient admission) | Yes ^{1,2} |
| Precertification with Medical Director Review Required | Yes ¹ |
| Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required) | Outpatient |

Special Considerations

¹Providers must call Oxford's Medical Management Department to obtain precertification, with required review by a Medical Director or their designee.

²New Jersey small group plan members should refer to their Certificate of Coverage for precertification and quantity limit guidelines.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member-specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to Oxford's [Acquired Rare Disease Drug Therapy Exception Process](#) policy.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

This policy provides information about the use of certain specialty pharmacy medications administered by either the subcutaneous (SC) or intravenous (IV) route.

This policy refers to the following drug products, which are interleukin-5 (IL-5) antagonists:

- Cinqair[®] (reslizumab)
- Fasentra[®] (benralizumab)
- Nucala[®] (mepolizumab)

Proven

Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Initial Therapy

Nucala for subcutaneous use is proven for the treatment of EGPA.¹

Nucala is medically necessary for the treatment of EGPA when all of the following criteria are met:

- Diagnosis of relapsing or refractory EGPA as defined by **all** of the following:¹³
 - Diagnosis with EPGA; **and**
 - Past medical history or presence of asthma; **and**
 - **One** of the following values at diagnosis:
 - Blood eosinophil level of at least 10% of leucocytes
 - Absolute eosinophil count > 1,000 cells/ μ L
- and**
- Presence of **at least two** of the following characteristics typical of EGPA:
 - Histopathological evidence of:
 - Eosinophilic vasculitis
 - Perivascular eosinophilic infiltration
 - Eosinophil-rich granulomatous inflammation
 - Neuropathy, mono or poly (motor deficit or nerve conduction abnormality)
 - Pulmonary infiltrates, non-fixed
 - Sino-nasal abnormality
 - Cardiomyopathy (established by echocardiography or MRI)

- Glomerulonephritis (hematuria, red cell casts, proteinuria)
 - Alveolar hemorrhage (by bronchoalveolar lavage)
 - Palpable purpura
 - Anti-neutrophil cytoplasmic antibody (ANCA) positive
- and**
- History of relapsing or refractory disease defined as **one** of the following:
 - Relapsing disease as defined as a past history (within the past 2 years) of at least one EGPA relapse (requiring additional or dose escalation of corticosteroids or immunosuppressant, or hospitalization).
 - Refractory disease as defined as failure to attain remission within the prior 6 months following induction treatment with standard therapy regimens; **and**
- and**
- Patient is currently taking standard therapy (corticosteroids with or without immunosuppressive therapy); **and**
 - Patient is **not** receiving Nucala in combination with either of the following:
 - Cinqair (reslizumab)
 - Fasenra (benralizumab)
 - Xolair (omalizumab)
- and**
- Nucala dosing for EGPA is in accordance with the U. S. Food and Drug Administration approved labeling: 300mg subcutaneously once every 4 weeks; **and**
 - Prescribed by or in consultation with a pulmonologist, rheumatologist, or allergist/immunologist; **and**
 - Initial authorization will be for no more than 6 months.

Reauthorization/Continuation of Care Criteria

For Nucala for the treatment of EGPA, authorization for continued use will be approved based on all of the following criteria:

- Documentation of positive clinical response as demonstrated by at least **one** of the following:
 - Reduction in the frequency and/or severity of relapses
 - Reduction or discontinuation of doses of corticosteroids and/or immunosuppressant
 - Disease remission
 - Reduction in severity or frequency of EGPA-related symptoms
- and**
- Patient is **not** receiving Nucala in combination with either of the following:
 - Cinqair (reslizumab)
 - Fasenra (benralizumab)
 - Xolair (omalizumab)
- and**
- Nucala dosing for EGPA is in accordance with the U. S. Food and Drug Administration approved labeling: 300mg subcutaneously once every 4 weeks; **and**
 - Prescribed by or in consultation with a pulmonologist, rheumatologist, or allergist/immunologist; **and**
 - Reauthorization will be for no more than 12 months.

Severe Asthma

Initial Therapy

Cinqair

Cinqair for intravenous use is proven for add-on therapy for patients who meet BOTH of the following criteria:²

- Have an eosinophilic phenotype
- Will be used as add-on maintenance therapy in the treatment of severe asthma

Cinqair is medically necessary when ALL of the following criteria are met:²⁻⁶

- Diagnosis of severe asthma; **and**
 - Classification of asthma as uncontrolled or inadequately controlled as defined by at least **one** of the following:
 - Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT score consistently less than 20); **or**
 - Two or more bursts of systemic corticosteroids for at least 3 days each in the previous 12 months; **or**
 - Asthma-related emergency treatment (e.g., emergency room visit, hospital admission, or unscheduled physician's office visit for nebulizer or other urgent treatment); **or**
 - Airflow limitation (e.g., after appropriate bronchodilator withhold FEV1 less than 80% predicted [in the face of reduced FEV1/FVC defined as less than the lower limit of normal]);
- and**
- Asthma is an eosinophilic phenotype as defined by a baseline (pre-reslizumab) peripheral blood eosinophil level of ≥ 400 cells/ μ L within the past 4 weeks; **and**
 - Used in combination with **one** of the following:

- **One** maximally-dosed (appropriately adjusted for age) combination ICS/LABA product [e.g., fluticasone propionate/salmeterol (Advair[®]), budesonide/formoterol (Symbicort[®])]; **or**
- Combination therapy including **both** of the following:
 - **One** high-dose (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco[®]), mometasone furoate (Asmanex[®]), beclomethasone dipropionate (QVAR[®])]; **and**
 - **One** additional asthma controller medication [e.g., LABA - olodaterol (Striverdi[®]) or indacaterol (Arcapta[®]), leukotriene receptor antagonist – montelukast (Singulair[®]), theophylline]

and

- Patient is **not** receiving Cinqair in combination with either of the following:

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

and

- Cinqair dosing for severe eosinophilic asthma is in accordance with the United States Food and Drug Administration approved labeling: 3 mg/kg intravenously once every 4 weeks; **and**
- Prescribed by or in consultation with a pulmonologist or allergist/immunologist; **and**
- Initial authorization will be for no more than 6 months.

Fasenra

Fasenra for subcutaneous use is proven for add-on therapy for patients who meet BOTH of the following criteria:

- Has an eosinophilic phenotype
- Will be used as add-on maintenance therapy in the treatment of severe asthma

Fasenra is medically necessary when ALL of the following criteria are met: ^{3, 5, 6, 10-12}

- Diagnosis of severe asthma; **and**
- Classification of asthma as uncontrolled or inadequately controlled as defined by at least **one** of the following:
 - Poor symptom control (e.g., Asthma Control Questionnaire [ACQ] score consistently greater than 1.5 or Asthma Control Test [ACT] score consistently less than 20); **or**
 - Two or more bursts of systemic corticosteroids for at least 3 days each in the previous 12 months; **or**
 - Asthma-related emergency treatment (e.g., emergency room visit, hospital admission, or unscheduled physician's office visit for nebulizer or other urgent treatment); **or**
 - Airflow limitation (e.g., after appropriate bronchodilator withhold forced expiratory volume in 1 second [FEV1] less than 80% predicted [in the face of reduced FEV1/forced vital capacity [FVC] defined as less than the lower limit of normal]);

and

- Asthma is an eosinophilic phenotype as defined by a baseline (pre- benralizumab treatment) peripheral blood eosinophil level ≥ 150 cells/ μ L within the past 6 weeks¹²; **and**
- Used in combination with **one** of the following:
 - **One** maximally-dosed (appropriately adjusted for age) combination inhaled corticosteroid (ICS)/long-acting beta₂-agonist (LABA) product [e.g., fluticasone propionate/salmeterol (Advair[®]), budesonide/formoterol (Symbicort[®])]; **or**
 - Combination therapy including **both** of the following:
 - **One** high-dose (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco[®]), mometasone furoate (Asmanex[®]), beclomethasone dipropionate (QVAR[®])]; **and**
 - **One** additional asthma controller medication [e.g., LABA - olodaterol (Striverdi[®]) or indacaterol (Arcapta[®]); leukotriene receptor antagonist – montelukast (Singulair[®]); theophylline]

and

- Patient is **not** receiving Fasenra in combination with either of the following:

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

and

- Fasenra dosing for severe eosinophilic asthma is in accordance with the United States Food and Drug Administration approved labeling: 30mg subcutaneously once every 4 weeks for 3 doses, then once every 8 weeks thereafter; **and**
- Prescribed by or in consultation with a pulmonologist or allergist/immunologist; **and**
- Initial authorization will be for no more than 6 months.

Nucala

Nucala for subcutaneous use is proven for add-on therapy for patients who meet BOTH of the following criteria:¹

- Has an eosinophilic phenotype

- Will be used as add-on maintenance therapy in the treatment of severe asthma

Nucala is medically necessary when ALL of the following criteria are met:^{1,3-6}

- Diagnosis of severe asthma; **and**
- Classification of asthma as uncontrolled or inadequately controlled as defined by at least **one** of the following:
 - Poor symptom control (e.g., Asthma Control Questionnaire [ACQ] score consistently greater than 1.5 or Asthma Control Test [ACT] score consistently less than 20); **or**
 - Two or more bursts of systemic corticosteroids for at least 3 days each in the previous 12 months; **or**
 - Asthma-related emergency treatment (e.g., emergency room visit, hospital admission, or unscheduled physician's office visit for nebulizer or other urgent treatment); **or**
 - Airflow limitation (e.g., after appropriate bronchodilator withhold forced expiratory volume in 1 second [FEV1] less than 80% predicted [in the face of reduced FEV1/forced vital capacity [FVC] defined as less than the lower limit of normal]);
- and**
- Asthma is an eosinophilic phenotype as defined by a baseline (pre-mepolizumab treatment) peripheral blood eosinophil level ≥ 150 cells/ μ L within the past 6 weeks; **and**
- Used in combination with **one** of the following:
 - **One** maximally-dosed (appropriately adjusted for age) combination inhaled corticosteroid (ICS)/long-acting beta₂-agonist (LABA) product [e.g., fluticasone propionate/salmeterol (Advair[®]), budesonide/formoterol (Symbicort[®])]; **or**
 - Combination therapy including **both** of the following:
 - **One** high-dose (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco[®]), mometasone furoate (Asmanex[®]), beclomethasone dipropionate (QVAR[®])]; **and**
 - **One** additional asthma controller medication [e.g., LABA - olodaterol (Striverdi[®]) or indacaterol (Arcapta[®]); leukotriene receptor antagonist – montelukast (Singulair[®]); theophylline]
- and**
- Patient is **not** receiving Nucala in combination with either of the following:
 - Cinqair (reslizumab)
 - Fasenna (beralizumab)
 - Xolair (omalizumab)
- and**
- Nucala dosing for severe eosinophilic asthma is in accordance with the United States Food and Drug Administration approved labeling: 100mg subcutaneously once every 4 weeks; **and**
- Prescribed by or in consultation with a pulmonologist or allergist/immunologist; **and**
- Initial authorization will be for no more than 6 months.

Reauthorization/Continuation of Care Criteria

For patients currently on Cinqair, Fasenna, or Nucala for the treatment of severe eosinophilic asthma, authorization for continued use will be approved based on **all** of the following criteria:

- Documentation of positive clinical response as demonstrated by at least **one** of the following:
 - Reduction in the frequency of exacerbations
 - Decreased utilization of rescue medications
 - Increase in percent predicted FEV1 from pretreatment baseline
 - Reduction in severity or frequency of asthma-related symptoms (e.g., wheezing, shortness of breath, coughing, etc.)
- and**
- Used in combination with an ICS-containing controller medication; **and**
- **One** of the following:
 - Patient is **not** receiving Nucala in combination with either of the following:
 - Cinqair (reslizumab)
 - Fasenna (beralizumab)
 - Xolair (omalizumab)
 - or**
 - Patient is **not** receiving Cinqair in combination with either of the following:
 - Fasenna (beralizumab)
 - Nucala (mepolizumab)
 - Xolair (omalizumab)
 - or**
 - Patient is **not** receiving Fasenna in combination with either of the following:
 - Cinqair (reslizumab)
 - Nucala (mepolizumab)
 - Xolair (omalizumab)
- and**

- **One** of the following:
 - Nucala dosing for severe eosinophilic asthma is in accordance with the United States Food and Drug Administration approved labeling: 100mg subcutaneously once every 4 weeks; **or**
 - Cinqair dosing for severe eosinophilic asthma is in accordance with the United States Food and Drug Administration approved labeling: 3 mg/kg intravenously once every 4 weeks; **or**
 - Fasenra dosing for severe eosinophilic asthma is in accordance with the United States Food and Drug Administration approved labeling: 30 mg subcutaneously once every 8 weeks;
- **and**
- Prescribed by or in consultation with a pulmonologist or allergist/immunologist; **and**
- Reauthorization will be for no more than 12 months.

Unproven/Not Medically Necessary

Cinqair, Fasenra, and Nucala are unproven and not medically necessary in the following:^{1-2,8}

- Other eosinophilic conditions
- Acute bronchospasm
- Status asthmaticus
- Chronic obstructive pulmonary disease (COPD)
- Granulomatosis with polyangiitis (Wegener's)
- Microscopic polyangiitis
- Organ or Life-threatening EGPA

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Cinqair (reslizumab)

Cinqair is approved by the U.S. Food and Drug Administration (FDA) for the add-on maintenance treatment of patients with severe asthma aged 18 years and older, who have an eosinophilic phenotype. Cinqair is not indicated for the treatment of other eosinophilic conditions or for acute bronchospasm or status asthmaticus. Because of the risk of anaphylaxis, healthcare providers administering Cinqair should observe patients closely for an appropriate period of time and be prepared to manage anaphylaxis that can be life-threatening.²

Fasenra (benralizumab)

Fasenra is approved by the U.S. Food and Drug Administration (FDA) for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, who have an eosinophilic phenotype. Fasenra is not indicated for the treatment of other eosinophilic conditions or for acute bronchospasm or status asthmaticus.¹⁰

Nucala (mepolizumab)

Nucala is approved by the U.S. Food and Drug Administration (FDA) for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, who have an eosinophilic phenotype. Nucala is not indicated for the treatment of other eosinophilic conditions or for acute bronchospasm or status asthmaticus. Nucala is also indicated for the treatment of adult patient with eosinophilic granulomatosis with polyangiitis (EGPA).¹

BACKGROUND

Asthma is a common chronic inflammatory disease of the airways that affects an estimated 24 million adults and children. Although the disease is well controlled with inhaled therapy in most patients, approximately 1.2-2.4 million people have severe asthma (i.e., 5-10% of the asthma population) that is associated with substantial morbidity, mortality, and economic effects. Asthma has been divided into subtypes, some of which are associated with airway inflammation with eosinophils. It is estimated that about half of individuals with severe asthma exhibit the eosinophilic phenotype with elevated eosinophil levels (a marker of inflammation) in both the blood and airways. Activated eosinophils can increase airway smooth muscle contraction and mucous secretion, which are hallmarks of asthma. Interleukin-5 (IL-5) is an important cellular signal in eosinophilic inflammation. Therapies that decrease IL-5 levels, such as Nucala (mepolizumab) and Cinqair (reslizumab), may decrease eosinophils in lung tissue. Fasenra (benralizumab) directly binds to the human IL-5 receptor on the surface of eosinophils and basophils, leading to the apoptosis of these cells through antibody-dependent cell mediated cytotoxicity.^{4,7,9,10}

Eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss syndrome) is characterized by asthma, sinusitis, pulmonary infiltrates, neuropathy, and eosinophilic vasculitis of one or more end organs. It is thought that eosinophils mediate the effects in patients with EGPA by infiltrating tissue and vasculature, causing inflammation. Systemic glucocorticoids are currently the standard of treatment for EGPA, however, some patients do not have sufficient response to therapy. Mepolizumab, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of mepolizumab action in asthma and EGPA has not been definitively established.^{1,13}

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

| HCPCS Code | Description |
|------------|-------------------------------|
| J0517 | Injection, benralizumab, 1 mg |
| J2182 | Injection, mepolizumab, 1 mg |
| J2786 | Injection, reslizumab, 1 mg |

| ICD-10 Diagnosis Code | Description |
|-----------------------|---|
| J45.50 | Severe persistent asthma, uncomplicated |
| J45.51 | Severe persistent asthma with (acute) exacerbation |
| J45.52 | Severe persistent asthma with status asthmaticus |
| J82 | Pulmonary eosinophilia, not elsewhere classified |
| M30.1 | Polyarteritis with lung involvement [Churg-Strauss] |

CLINICAL EVIDENCE

Proven/Medically Necessary

Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Mepolizumab is indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).¹

In a multicenter, double-blind, parallel-group, phase 3 trial, Wechsler et al, evaluated the efficacy and safety mepolizumab versus placebo for eosinophilic granulomatosis with polyangiitis (EGPA).¹³ Patients with relapsing or refractory EGPA were randomly assigned to receive 300 mg of mepolizumab (n=68) or placebo (n=68) subcutaneously every 4 weeks, plus standard care, for 52 weeks. Patients had to have received treatment for at least 4 weeks and were taking stable corticosteroid dosing for at least 4 weeks. The two primary end points were the accrued weeks of remission over the 52 week period, and the proportion of participants in remission at both week 36 and week 48. Secondary endpoints included: time to first relapse and average daily glucocorticoid use at weeks 48 through 52). Patients receiving mepolizumab had significantly more accrued weeks of remission than placebo (28% vs. 3% had 24 weeks of accrued remission; odds ratio, 5.91; 95% confidence interval [CI], 2.68 to 13.03; P<0.001) and a higher percentage of patients were in remission at both week 36 and week 48 (32% vs. 3%; odds ratio, 16.74; 95% CI, 3.61 to 77.56; P<0.001). Remission did not occur in 47% of the patients in the mepolizumab group versus 81% of those in the placebo group. The annualized relapse rate was 1.14 in the mepolizumab group, as compared with 2.27 in the placebo group (rate ratio, 0.50; 95% CI, 0.36 to 0.70; P<0.001). A total of 44% of the patients in the mepolizumab group, as compared with 7% of those in the placebo group, had an average daily dose of prednisolone or prednisone of 4.0 mg or less per day during weeks 48 through 52 (odds ratio, 0.20; 95% CI, 0.09 to 0.41; P<0.001). The authors concluded that in patients with EGPA, mepolizumab resulted in significantly more weeks in remission and a higher proportion of patients in remission than placebo, although only half of the patients treated with mepolizumab had protocol-defined remission.

Severe Eosinophilic Asthma

Benralizumab is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.¹⁰

Mepolizumab is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype.¹

Reslizumab is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype.²

Professional Societies

The Global Initiative for Asthma (GINA)

The Global Initiative for Asthma (GINA, 2018) recommends that for Step 5 treatment, adults and adolescents, may be treated with **mepolizumab** or **reslizumab**) as follows (Evidence A: Randomized controlled trials and meta-

analyses. Rich body of evidence ⁶Step 5: Higher level care and/or add-on treatment. Patients with persistent symptoms or exacerbations despite correct inhaler technique and good adherence with Step 4 treatment and in whom other controller options have been considered, should be referred to a specialist with expertise in management of severe asthma (Evidence D: Panel consensus judgment).

Add-on anti-interleukin- treatment (subcutaneous mepolizumab for patients aged ≥ 12 years; intravenous reslizumab for ages ≥ 18 years) or anti-interleukin 5 receptor treatment (subcutaneous benralizumab for ages ≥ 12 years), with severe eosinophilic asthma that is uncontrolled on Step 4 treatment. (Evidence A)

Institute for Clinical and Economic Review (ICER)

On March 14, 2016, the Institute for Clinical and Economic Review (ICER) released a clinical report entitled, "Mepolizumab (Nucala[®], GlaxoSmithKline plc.) for the Treatment of Severe Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks." ICER recommendations are as follows: ⁴

- ICER judges the current body of evidence on **mepolizumab** to be "comparable or better."
- For adult patients with severe eosinophilic asthma, ICER judges there to be moderate certainty of a comparable or better net benefit for **mepolizumab** 100mg SC every four weeks as add-on maintenance treatment compared with standard of care including high dose ICS, LABA, and additional controller medications. There is moderate certainty because both the MENSA trial, which demonstrated a significant reduction in asthma exacerbations, and the SIRIUS trial, which demonstrated a significant reduction in oral corticosteroids dosage, were relatively small studies of short duration. There remains uncertainty about the long-term durability of the benefits of the therapy and about the potential harms from modulation of the immune system. Ongoing post-marketing trials and extension studies evaluating **mepolizumab** may demonstrate a wide variety of outcomes, from substantial net health benefit to a comparable net benefit given the potential harms associated with the monoclonal antibody (opportunistic infection, anaphylaxis).

European Respiratory Society (ERS)/American Thoracic Society (ATS)

The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines define severe asthma as that which requires treatment with high-dose ICSs plus a second controller (or systemic corticosteroids) to prevent progression to uncontrolled disease status or continuing uncontrolled disease status despite this therapy.³ The guidelines recommend that, "While the anti-IL5 antibody, mepolizumab, was not beneficial in unselected adult patients with moderate asthma, when studied in severe asthma patients with persistent sputum eosinophilia, two anti-IL-5 antibodies, mepolizumab and reslizumab, have been shown to decrease exacerbations and oral corticosteroid use, as well as improve symptoms and lung function to varying degrees."

Unproven/Not Medically Necessary

Nucala and Cinqair have additional uses listed in the FDA-label:¹⁻²

- Other eosinophilic conditions
- Acute bronchospasm
- Status asthmaticus
- Chronic obstructive pulmonary disease (COPD)

Statistically robust randomized controlled trials are necessary to establish the safety and efficacy of Fasenra, Nucala and Cinqair to treat these conditions.^{1-2,8,10}

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee. [2018D0055E]

1. Nucala[®] [prescribing information]. Research Triangle Park, NC; GlaxoSmithKline, LLC; December 2017.
2. Cinqair[®] [prescribing information]. Frazer, PA; Teva Respiratory, LLC; May 2016.
3. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014 Feb;43(2):343-73.
4. Institute for Clinical and Economic Review (ICER). Mepolizumab (Nucala[®], GlaxoSmithKline plc.) for the Treatment of Severe Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks. March 14, 2016. Available at <http://icer-review.org/material/asthma-final-report/>. Accessed April 25, 2016.
5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2017. Available at <http://www.ginasthma.org>. Accessed June 19, 2017.
6. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, et al. Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma. *New Eng J Med*. 2014 Sept;371(13):1189-97.

7. Parameswaran KN, Dasgupta A, et al. Mepolizumab in COPD with Eosinophilic Bronchitis: A Randomized Clinical Trial. Poster session presented at the Annual Meeting of the American Academy of Allergy, Asthma and Immunology, Los Angeles, CA. March 6, 2016.
8. Centers for Disease Control and Prevention. Asthma. Available at <http://www.cdc.gov>. Accessed May 16, 2016.
9. National Heart, Lung and Blood Institute. Explore Asthma. Available at <http://www.nhlbi.nih.gov>. Accessed May 16, 2016.
10. Fasenra® [prescribing information]. Wilmington, DE; AstraZeneca Pharmaceuticals LP; November 2017
11. FitzGerald JM, Bleecker ER, Menzies-Gow A, et al. Predictors of enhanced response with benralizumab for patients with severe asthma: pooled analysis of the SIROCCO and CALIMA studies. *Lancet Respir Med*. 2017 Sep 8.
12. Goldman M, Hirsch I, Zangrilli JG, et al. The association between blood eosinophil count and benralizumab efficacy for patients with severe, uncontrolled asthma: subanalyses of the Phase III SIROCCO and CALIMA studies. *Curr Med Res Opin*. 2017 Sep;33(9):1605-1613.
13. Wechsler ME, Akuthota P, Jayne D, et al. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. *N Engl J Med* 2017; 376: 1921-32.

POLICY HISTORY/REVISION INFORMATION

| Date | Action/Description |
|------------|--|
| 01/01/2019 | <ul style="list-style-type: none"> • Updated list of applicable HCPCS codes to reflect annual code edits; added J0517 • Archived previous policy version PHARMACY 293.6 T2 |