Corporate Medical Policy: Interleukin-5 Antagonists **"Notification"** **POLICY EFFECTIVE JANUARY 1, 2025**

Restricted Product(s):

- benralizumab (Fasenra®) subcutaneous injection for administration by a healthcare professional
- mepolizumab (Nucala®) subcutaneous injection for administration by a healthcare professional
- reslizumab (Cinqair®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- Benralizumab (Fasenra®)
  - Add-on maintenance treatment for severe asthma in adults and children 6 years or older with an eosinophilic phenotype
  - Treatment of adults with eosinophilic granulomatosis with polyangiitis (EGPA)
  - Limitations of use: Not for relief of acute bronchospasm or status asthmaticus

- Mepolizumab (Nucala®)
  - Add-on maintenance treatment for severe asthma in adults and children 6 years or older with an eosinophilic phenotype
  - Treatment of adults with eosinophilic granulomatosis with polyangiitis (EGPA)
  - Treatment of adults and children 12 years or older with hypereosinophilic syndrome (HES) for at least 6 months without an identifiable non-hematologic secondary cause
  - Add-on maintenance treatment of adult patients 18 years or older with chronic rhinosinusitis with nasal polyps (CRSwNP)
  - Limitations of use: Not for relief of acute bronchospasm or status asthmaticus

- Reslizumab (Cinqair®)
  - Add-on maintenance treatment for severe asthma in patients 18 years or older with an eosinophilic phenotype
  - Limitations of use: Not for treatment of other eosinophilic conditions or for relief of acute bronchospasm or status asthmaticus

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

*For patients that are new to the plan and currently using the medication, the criteria pertain to when the patient started the medication.

1. The patient has a diagnosis of severe **eosinophilic asthma**; **AND**
    a. The patient is 18 years of age or older; **OR**
    b. If the request is for benralizumab (Fasenra) or mepolizumab (Nucala), the patient is 6 years of age or older; **AND**
    c. The patient has one of the following:
        i. If the request is for benralizumab (Fasenra) or mepolizumab (Nucala):
            1. Eosinophil counts greater than or equal to 150 cells/microliter at initiation of therapy (i.e., within the past 6 weeks); **OR**
            2. Eosinophil counts greater than or equal to 300 cells/microliter in the past 12 months; **AND**
        ii. If the request is for reslizumab (Cinqair):
            1. Eosinophil counts greater than or equal to 400 cells/microliter at initiation of therapy (i.e., within the past 6 weeks); **OR**
            2. Eosinophil counts greater than or equal to 400 cells/microliter in the past 12 months; **AND**
    d. The patient does NOT have neoplastic disease or known/suspected parasitic infection; **AND**
    e. The patient has had two or more exacerbations in the past year despite adherence to therapy with:
        i. 12 months of high-dose inhaled corticosteroid (ICS) given in combination with a minimum of 3 months of controller medication (either a long-acting beta2-agonist [LABA], or leukotriene receptor antagonist [LTRA], or theophylline), unless the patient is intolerant of, or has a medical contraindication to these medications; **OR**
        ii. 6 months of ICS with daily oral glucocorticoids given in combination with a minimum of 3 months of controller medication (either a LABA, or LTRA, or theophylline), unless the patient is intolerant of, or has a medical contraindication to these medications; **OR**

2. The patient has a diagnosis of **eosinophilic granulomatosis with polyangiitis (EGPA/Churg-Strauss Syndrome)**; **AND**
    a. The request is for benralizumab (Fasenra) or mepolizumab (Nucala); **AND**
    b. The patient is 18 years of age or older; **AND**
    c. The patient is stable on oral corticosteroids; **AND**

d. The patient has tried and failed or has a clinical intolerance/contraindication to an oral immunosuppressant (e.g., cyclophosphamide, azathioprine, methotrexate, leflunomide, mycophenolate mofetil); **OR**

3. The patient has a diagnosis of **hypereosinophilic syndrome (HES)**; **AND**
    a. The request is for mepolizumab (Nucala); **AND**
    b. The patient is 12 years of age or older; **AND**
    c. The patient has been diagnosed for six months or greater; **AND**
    d. The patient does NOT have non-hematologic secondary HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy) or FIP1L1-PDGFRα kinase-positive HES; **AND**
    e. The patient has been on stable dosing of and will continue HES therapy (e.g., oral corticosteroids, immunosuppressive agents and/or cytotoxic therapy); **AND**
    f. The patient has had at least two HES flares in the past 12 months (one of which was NOT related to a decrease in HES therapy within 4 weeks prior to flare) defined as:
        i. HES-related worsening of clinical symptoms; **OR**
        ii. Blood eosinophil count requiring escalation in therapy; **AND**
    g. The patient has a blood eosinophil count greater than or equal to 1,000 cells/microliter; **OR**

4. The patient has a diagnosis of **chronic rhinosinusitis with nasal polyposis (CRSwNP)**; **AND**
    a. The request is for mepolizumab (Nucala); **AND**
    b. The patient is 18 years of age or older; **AND**
    c. The patient has tried and failed or has a clinical intolerance/contraindication to Xhance (fluticasone propionate nasal spray) **[medical record documentation required]**; **OR**
    d. The patient has tried and failed or has a clinical intolerance/contraindication to oral systemic corticosteroids within the previous 6 months **[medical record documentation required]**; **AND**
    e. ONE of the following:
        i. The patient has had prior surgery for nasal polyps **[medical record documentation required]**; **OR**
        ii. The patient is not a candidate for sinus surgery **[medical record documentation required]**; **AND**
    f. The patient will not be using Nucala (mepolizumab) in combination with Xhance (fluticasone propionate nasal spray); **AND**
    g. ONE of the following:
        i. The patient is currently being treated with an over the counter intranasal steroid; **OR**
        ii. The patient has a clinical intolerance/contraindication to ALL intranasal steroids **[medical record documentation required]**; **AND**

5. The patient will NOT receive the requested agent in combination with another biologic immunomodulator agent used for the same indication [e.g., benralizumab (Fasenra), dupilumab (Dupixent), mepolizumab (Nucala), omalizumab (Xolair), reslizumab (Cinqair)]; **AND**
6. For reslizumab (Cinqair) requests, ONE of the following:
    a. The patient has tried and had an inadequate response to the provider-administered formulations of benralizumab (Fasenra) AND mepolizumab (Nucala) **[medical record documentation required]**; **OR**
    b. The patient has a clinical intolerance, FDA labeled contraindication, or hypersensitivity to the provider-administered formulations of benralizumab (Fasenra) AND mepolizumab (Nucala) **[medical record documentation required]**; **AND**
7. For mepolizumab (Nucala) or benralizumab (Fasenra) requests, the patient has a physical or cognitive limitation that makes the utilization of a self-administered formulation unsafe or otherwise not feasible, as demonstrated by BOTH of the following **[medical record documentation required]**:
    a. Inability to self-administer the medication; **AND**
    b. Lack of caregiver or support system for assistance with administration of self-administered products; **AND**
8. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
9. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

    Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. For patients with a diagnosis of severe **eosinophilic asthma**, they have demonstrated one or more of the following while using the medication **[medical record documentation required]**:
    a. Decreased utilization of rescue medications;
    b. Decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in ICS dose or treatment with systemic corticosteroids);
    c. Increase in predicted FEV1 from pretreatment baseline;
    d. Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing; **OR**
4. For patients using benralizumab (Fasenra) or mepolizumab (Nucala) for **eosinophilic granulomatosis with polyangiitis**, the patient is stable on oral corticosteroid therapy; **OR**

5. For patients using mepolizumab (Nucala) for **hypereosinophilic syndrome (HES)**, they have demonstrated one or more of the following while using the medication **[medical record documentation required]**:
    a. Reduction in number of flares from baseline; **OR**
    b. Improvement in clinical symptoms (e.g., fatigue severity, cough, breathlessness); **OR**
6. For patients using mepolizumab (Nucala) for **chronic rhinosinusitis with nasal polyposis (CRSwNP)**:
    a. The patient has been on and adherent to an over the counter intranasal steroid since starting mepolizumab (Nucala) therapy **[medical record documentation required]**; **OR**
    b. The patient has a clinical intolerance/contraindication to ALL intranasal steroids **[medical record documentation required]**; **AND**

7. The patient will NOT receive the requested agent in combination with another biologic immunomodulator agent used for the same indication [e.g., benralizumab (Fasenra), dupilumab (Dupixent), mepolizumab (Nucala), omalizumab (Xolair), reslizumab (Cinqair)]; **AND**
8. For reslizumab (Cinqair) requests, ONE of the following:
    a. The patient has tried and had an inadequate response to the provider-administered formulations of benralizumab (Fasenra) AND mepolizumab (Nucala) **[medical record documentation required]**; **OR**
    b. The patient has a clinical intolerance, FDA labeled contraindication, or hypersensitivity to the provider-administered formulations of benralizumab (Fasenra) AND mepolizumab (Nucala) **[medical record documentation required]**; **AND**
9. For mepolizumab (Nucala) or benralizumab (Fasenra) requests, the patient has a physical or cognitive limitation that makes the utilization of a self-administered formulation unsafe or otherwise not feasible, as demonstrated by BOTH of the following **[medical record documentation required]**:
    a. Inability to self-administer the medication; **AND**
    b. Lack of caregiver or support system for assistance with administration of self-administered products; **AND**
10. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
11. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

    Duration of Approval: 365 days (1 year)

FDA Label Reference				
Medication	**Indication*,^**	**Dosing**	**HCPCS**	**Maximum Units***
benralizumab (Fasenra®) subcutaneous (SC) injection	Severe asthma in patients ≥6 years old EGPA in adults	Asthma: 6 to 11 years: • Weight < 35 kg: 10 mg SC every 4 weeks x 3 doses, then 10 mg every 8 weeks • Weight ≥ 35 kg: 30 mg SC every 4 weeks x 3 doses, then 30 mg every 8 weeks ≥12 years: 30 mg SC every 4 weeks x 3 doses, then 30 mg every 8 weeks EGPA: 30 mg SC every 4 weeks	J0517	Asthma: 240 EGPA: 390
mepolizumab (Nucala®) subcutaneous (SC) injection	Severe asthma in patients ≥6 years old EGPA in adults HES in patients ≥12 years old	Asthma: 6 to 11 years: 40 mg SC every 4 weeks ≥12 years: 100 mg SC every 4 weeks EGPA: 300 mg (3 separate 100 mg injections) SC every 4 weeks HES: 300 mg (3 separate 100 mg injections) SC every 4 weeks	J2182	Asthma: 1300 EGPA: 3900 HES: 3900 CRSwNP: 1300

FDA Label Reference				
Medication	**Indication*,^**	**Dosing**	**HCPCS**	**Maximum Units***
	CRSwNP in adults	CRSwNP: 100 mg SC every 4 weeks		
reslizumab (Cinqair®) intravenous (IV) infusion	Severe asthma in patients ≥18 years old	IV: 3 mg/kg every 4 weeks	J2786	3900

* Not indicated for treatment of other eosinophilic conditions or for relief of acute bronchospasms or status asthmaticus
^ Benralizumab, mepolizumab and reslizumab have not been studied for use in combination with Xolair (omalizumab)

***Maximum units allowed for duration of approval**

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
    b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
    c. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
    d. Re-initiation of therapy, defined as ONE of the following:
        i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
        ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
    e. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

January 2025: Criteria change (Cinqair): Added requirement for trial and failure of the provider-administered formulations of Fasenra and Nucala prior to use of Cinqair within initial and continuation criteria. Adjusted maximum units for Cinqair according to FDA labeled dosing. **Policy notification given 11/1/2024 for effective date 1/1/2025**.
October 2024: Criteria change: Added newly approved indication for Fasenra for adults with eosinophilic granulomatosis with polyangiitis (EGPA) with corresponding criteria and associated dosing in FDA label reference table. For EGPA indication, removed requirement for having diagnosis for six months or greater.
September 2024: Criteria update: For eosinophilic asthma indication, expanded criteria for eosinophil counts at initiation of therapy to allow for within the past 6 weeks for clarity. Other minor adjustments made to FDA label reference table formatting for clarity with no change to policy intent.
May 2024: Criteria update (Fasenra): Expanded eosinophilic asthma indication to include patients 6 years of age and older per updated FDA label and updated FDA label reference table with corresponding dosing.
January 2023: Criteria update: Added requirement within initial criteria for asthma indication that patient must be adherent to conventional therapies. Corrected typographical, formatting, and criteria errors within policy for CRSwNP indication with no change to policy intent. **Policy notification given 11/1/2022 for effective date 1/1/2023**.
February 2022: Criteria change: Added indication for Nucala of chronic rhinosinusitis with nasal polyposis with initial and continuation criteria for approval and updated dosing table/max units with new indication.
August 2021: Criteria update: Removed hypereosinophilic syndrome exclusion from eosinophilic asthma initial criteria.
April 2021: Criteria change: Added requirement of a trial and failure of an oral immunosuppresant for diagnosis of EGPA/Churg-Strauss Syndrome prior to Nucala use; added continuation criteria for HES indication; added maximum units; medical policy formatting change. **Policy notification given 2/26/2021 for effective date 4/28/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.