Interleukin-5 (IL-5) Inhibitors Medical Drug Criteria with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
3/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Cinqair® (reslizumab) Injection for intravenous use	Add-on maintenance treatment of patients with severe asthma aged 18 years and older with an eosinophilic phenotype Limitation of use: Not indicated for treatment of other eosinophilic conditions, or relief of acute bronchospasm or status asthmaticus		2
Fasenra® (benralizumab) Injection for subcutaneous use	Add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype Limitation of use: Not indicated for treatment of other eosinophilic conditions, or relief of acute bronchospasm or status asthmaticus		3
Nucala® (mepolizumab) Injection for subcutaneous use	Add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype Limitation of use: Not indicated for treatment of other eosinophilic conditions, or relief of acute bronchospasm or status asthmaticus Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA) Treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥ 6 months without an identifiable non-hematologic secondary cause Add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Asthma	Asthma is a chronic inflammatory disorder of the airways.(4,6) It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.(4) Symptoms of asthma include wheezing, coughing, recurrent difficulty breathing, shortness of breath, and chest tightness. Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles. Guidelines recommend the use of detailed medical history, physical examination, and spirometry to make a diagnosis of asthma.(4,6)
	
	The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma. Long-term goals for asthma management are to achieve good control of symptoms, maintain normal activity level, and to minimize the future risk of exacerbations, fixed airflow limitation, and side-effects.(6) IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with low dose inhaled corticosteroids (ICS) in combination with a long-acting beta agonist (LABA). Severe asthma is defined as asthma that requires Step 4 or 5 treatment (e.g., with high dose ICS plus a LABA) to prevent it from becoming 'uncontrolled' or which remains uncontrolled despite this therapy. Early initiation of low dose ICS in patients with asthma has led to greater improvement in lung function than initiation of ICS after symptoms have been present for more than 2 to 4 years. The 2022 GINA guidelines recommend every adult and adolescent with asthma should receive ICS-containing controller medication to reduce the risk of serious exacerbation, even in patients with infrequent symptoms.(6)
	
	2022 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations and are broken into two tracks based on reliever therapy.
	
	Track 1 is the preferred approach recommended by GINA, because using low dose ICS-formoterol as reliever reduces the risk of severe exacerbations compared with regimens with SABA as reliever, with similar symptom control:(6)
	
	• Step 1: As-needed low dose ICS-formoterol
	• Step 2: As-needed low dose ICS-formoterol
	  ○ Alternative options: Daily leukotriene receptor antagonist (LTRA), or add house dust mite (HDM) sublingual immunotherapy (SLIT)
	  ○ LTRA are less effective than ICS, particularly for preventing exacerbations
	• Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up
	  ○ Preferred controller: Low dose maintenance ICS-formoterol
	  ○ Reliever: As-needed low dose ICS-formoterol
	  ○ Alternative options: Medium dose ICS, or add LTRA, or add HDM SLIT
	• Step 4: Medium dose maintenance ICS-formoterol
	  ○ Reliever: As-needed low dose ICS-formoterol
	  ○ Alternative options: Add long-acting muscarinic antagonist (LAMA) or LTRA, or switch to high dose ICS
	• Step 5: Add-on LAMA; refer for phenotypic assessment and consider high dose ICS-formoterol with add on anti-IgE, anti-IL5/5R, anti-IL4R, or anti-TSLP
	  ○ Reliever: As-needed low dose ICS-formoterol

	○ Alternative options: Add azithromycin (adults) or LTRA; add low dose oral corticosteroids (OCS) but consider side effects **Track 2** is an alternative approach if Track 1 is not possible or is not preferred by a patient with no exacerbations on their current therapy. Before considering a regimen with SABA reliever, the clinician should consider whether the patient is likely to be adherent with their controller therapy; if not, they will be exposed to the risks of SABA-only treatment:(6) • Step 1: Take ICS whenever SABA taken ○ Reliever: As-needed short-acting β-2 agonist (SABA) • Step 2: Low dose maintenance ICS ○ Reliever: As-needed SABA ○ Alternative options: Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT ○ LTRA are less effective than ICS, particularly for preventing exacerbations • Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up ○ Preferred controller: Low dose maintenance ICS-LABA ○ Reliever: As-needed SABA ○ Alternative options: Medium dose ICS, or add LTRA, or add HDM SLIT • Step 4: Medium/high dose maintenance ICS-LABA ○ Reliever: As-needed SABA ○ Alternative options: Add LAMA or LTRA, or switch to high dose ICS • Step 5: Add-on LAMA; refer for phenotypic assessment and consider high dose ICS-LABA with add on anti-IgE, anti-IL5/5R, anti-IL4R, or anti-TSLP ○ Reliever: As-needed SABA ○ Alternative options: Add azithromycin (adults) or LTRA; add low dose oral corticosteroids (OCS) but consider side effects 2022 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:(6) • Step 1: low dose ICS taken whenever SABA taken ○ Reliever: as needed SABA (or ICS-formoterol reliever for maintenance and reliever therapy [MART]) ○ Alternative controller: daily low dose ICS (likelihood of poor adherence should be taken into account) • Step 2: daily low dose ICS ○ Reliever: as needed SABA (or ICS-formoterol reliever for MART) ○ Alternative options: Leukotriene receptor antagonist (LTRA) or as needed ICS taken at the same time as a SABA ○ LTRA are less effective than ICS, particularly for preventing exacerbations • Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up ○ Preferred controller: low dose ICS-LABA OR medium dose ICS OR very lose dose ICS-formoterol MART ○ Reliever: as needed SABA (or ICS-formoterol reliever for MART) ○ Alternative controller: low dose • Step 4: medium dose ICS-LABA OR low dose ICS-formoterol MART ○ Reliever: as needed SABA (or ICS-formoterol reliever for MART) ○ Alternative options: add-on tiotropium or add-on LTRA ○ Refer for expert advice • Step 5: refer for phenotypic assessment with or without higher dose ICS-LABA or add on therapy with anti-IgE or anti-IL4R

- Reliever: as needed SABA (or ICS-formoterol reliever for MART)
- Alternative options: add-on anti-IL5/5R (i.e., mepolizumab), or as a last resort consider add on low dose OCS but consider side effects

Severe Asthma Phenotype and Eosinophilic Asthma Subphenotype

Severe asthma is defined by GINA guidelines as asthma that is uncontrolled despite adherence with maximal optimized GINA Step 4 or Step 5 therapy (e.g., medium or high dose ICS with a second controller; maintenance OCS) and treatment of contributory factors (e.g., inhaler technique, smoking or comorbidities), or that worsens when high dose treatment is decreased. Roughly 3% to 10% of adults with asthma have severe asthma.(6) The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014; updated 2020) and the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group mirror the GINA definition of severe asthma, and defined uncontrolled asthma for adult and pediatric patients 5 years of age and over:(4,21)

- Frequent severe exacerbations (i.e., two or more bursts of systemic corticosteroids within the past 12 months)
- Serious exacerbations (i.e., at least one hospitalization, intensive care unit stay, or mechanical ventilation in the past 12 months)
- Airflow limitation (i.e., FEV1 less than 80% predicted)
- Asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids

A specialist, preferably in a multidisciplinary severe asthma clinic (if available) performs further assessment, which includes the patient's inflammatory phenotype (i.e., Type 2 or non-Type 2).(6)

Type 2 inflammation is characterized by the presence of cytokines such as interleukin (IL)-4, IL-5, and IL-13, which are often produced by the adaptive immune system on recognition of allergens. It is also characterized by eosinophilia or increased fraction of exhaled nitric oxide (FeNO) and may be accompanied by atopy. In many patients with asthma, Type 2 inflammation rapidly improves when ICS are taken regularly and correctly; this is classified as mild or moderate asthma. In severe asthma, Type 2 inflammation may be relatively refractory to high dose ICS. Type 2 inflammation is considered refractory if any of the following are found while the patient is taking high dose ICS or daily OCS:(6)

- Blood eosinophils greater than or equal to 150 cells/microliter
- FeNO greater than or equal to 20 ppb
- Sputum eosinophils greater than or equal to 2%
- Asthma is clinically allergen-driven

Biologic agents should be considered as add-on therapy for patients with refractory Type 2 inflammation with exacerbations or poor symptom control despite taking at least high dose ICS/LABA, and who have allergic or eosinophilic biomarkers or need maintenance OCS.(6) 2022 GINA recommends the biologics below based on patient eligibility factors:

- Anti-IgE (omalizumab):

	○ Sensitization on skin prick testing or specific IgE ○ Total serum IgE and weight within dosage range ○ Exacerbations in the last year • Anti-IL5/Anti-IL5R (benralizumab, mepolizumab, reslizumab): ○ Exacerbations in the last year ○ Blood eosinophils greater than or equal to 150 cells/microliter (for benralizumab and mepolizumab) or greater than or equal to 300 cells/microliter (for reslizumab) • Anti-IL4R (dupilumab): ○ Exacerbations in the last year ○ Blood eosinophil greater than or equal to 150 cells/microliter but less than or equal to 1500 cells/microliter, or FeNO greater than or equal to 25 ppb, or taking maintenance OCS • Anti-TSLP (tezepelumab): ○ Exacerbations in the last year Patient response should be evaluated 4 months after initiating therapy and follow up should occur every 3 to 6 months thereafter. 2022 GINA recommends the following step-down therapy process in patients responding well to targeted biologic therapy:(6) • Reevaluate the need for each asthma medication every 3 to 6 months, but inhaled therapy should not be completely stopped • Oral treatments: gradually decreased starting with OCS due to significant adverse effects. • Inhaled treatments: consider reducing ICS dose after 3 to 6 months, but do not completely stop inhaled therapy. Continue at least medium dose ICS and remind patients of the importance of continued inhaled controller therapy • Biologic treatments: trial withdrawal after 12 months of treatment and only if patient's asthma remains well controlled on medium dose ICS, and for allergic asthma, there is no further exposure to a previous allergic trigger **Cinqair Efficacy** The efficacy of Cinqair (reslizumab) was established in four randomized, double-blind, placebo-controlled studies. All subjects continued their background asthma therapy throughout the duration of the studies. The primary endpoint for studies I and II was asthma exacerbation frequency. Patients had significant reductions in the rate of all exacerbations compared to placebo (requiring the use of OCS or hospitalization). The proportion of patients who did not experience an asthma exacerbation during the 52-week treatment period was higher in the Cinqair group compared to placebo. All four studies showed significant reductions in FEV (the primary endpoint for studies III and IV), with improvements observed at week 4 following the first dose and maintained through week 52 for studies I and II. Studies I, II, and III required the trial patients to have a blood eosinophil count of at least 400 cells/microliter at screening (within 3-4 weeks of initiation). Study IV included patients with poorly controlled asthma who were unselected for eosinophil count.(2) In an attempt to identify the eosinophil threshold that would maximize benefit, Cinqair efficacy was examined in a population unselected for eosinophil count. No differences between Cinqair and placebo were observed with respect to the overall population, but in patients with greater than or equal to 400 cells/microliter clinically meaningful improvements were observed versus placebo in the primary endpoint, FEV1 at Week

16 weeks, as well as in ACQ-7, rescue medication use, and FVC. No meaningful trends were observed in patients with fewer than 400 cells/microliter.(2,19)

Fasenra Efficacy

Benralizumab was approved through 3 confirmatory clinical trials. Trial 1 and Trial 2 were exacerbation trials in patients 12 years of age and older. All subjects continued their background asthma therapy throughout the duration of the trials. The primary endpoint was the rate of asthma exacerbations in patients who were taking high-dose ICS and LABA. Asthma exacerbation was defined as a worsening of asthma requiring use of oral/systemic corticosteroids for at least 3 days, and/or emergency department visits requiring use of oral/systemic corticosteroids and/or hospitalization. For patients on maintenance oral corticosteroids, an asthma exacerbation requiring oral corticosteroids was defined as a temporary increase in stable oral/systemic corticosteroids for at least 3 days or a single depo-injectable dose of corticosteroids. In Trial 1, 35% of patients receiving benralizumab experienced an asthma exacerbation compared to 51% on placebo. In Trial 2, 40% of patients receiving benralizumab experienced an asthma exacerbation compared to 51% on placebo.(3)

Trial 3 was a randomized OCS reduction trial in asthma patients. Patients were required to be treated with daily OCS (7.5 to 40 mg per day) in addition to regular use of high-dose ICS and LABA with or without additional controller(s). The trial included an 8-week run-in period during which the OCS was titrated to the minimum effective dose without losing asthma control. For the purposes of the OCS dose titration, asthma control was assessed by the investigator based on a patient's FEV1, peak expiratory flow, nighttime awakenings, short-acting bronchodilator rescue medication use or any other symptoms that would require an increase in OCS dose. Fasenra achieved greater reductions in daily maintenance OCS dose while maintaining asthma control compared to placebo (median reduction of 75% for Fasenra vs 25% for placebo).(3)

Nucala Efficacy

The efficacy of mepolizumab for the treatment of severe eosinophilic asthma was established in three double-blind, randomized, placebo-controlled trials: A dose-ranging and exacerbation reduction trial (trial 1) and two confirmatory trials (trial 2 and 3). All subjects continued their background asthma therapy throughout the duration of the trials. Trial 1 enrolled subjects with uncontrolled asthma despite use of high dose inhaled corticosteroids (ICS) plus additional controller(s), with or without OCS. Trial 2 was a placebo- and active-controlled trial in subjects with asthma not adequately controlled on high-dose inhaled corticosteroids plus additional controller(s) with or without OCS. The primary end point for trial 1 and 2 was frequency of asthma exacerbations. Compared to placebo, subjects receiving mepolizumab experienced significantly fewer exacerbations and had a longer time to first exacerbation.(1)

Trial 3 was an OCS-reduction study in asthma patients who required daily OCS in addition to regular controller medications. The primary end point was percent reduction of OCS dose during weeks 20 to 24 without loss of asthma control. The baseline mean oral corticosteroid use was similar between the Nucala and placebo group. Overall, mepolizumab achieved greater reduction in oral corticosteroid use while maintaining asthma control when compared to placebo. However, the difference between the mepolizumab and placebo groups was not statistically significant.(1)

Eosinophilic Granulomatosis with Polyangiitis (EGPA)	Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss Syndrome, is a rare systemic vasculitis disease with main clinical features of late-onset allergic rhinitis and asthma, increased blood eosinophil count, and vasculitis manifestations, some of which can be life threatening.(7) Once EGPA is suspected based on clinical findings of asthma with eosinophilia, asthma with systemic manifestations, or even eosinophilia with extrapulmonary disease, a biopsy demonstrating small or medium sized vessel vasculitis strongly supports the diagnosis of EGPA. Skin, nerve, and muscle are among the most common biopsied tissues, but endomyocardial, renal, and gastrointestinal biopsies may also be useful. Antineutrophil cytoplasm antibody (ANCA) testing is also recommended. ANCA positivity is highly suggestive of EGPA, but ANCA negative results do not rule out its diagnosis.(7) There are two types of classifications used for the diagnosis of EGPA. The first and most commonly used classification is by the American College of Rheumatology (ACR). ACR has established six criteria for the classification of EGPA in a patient with documented vasculitis. The presence of four or more of these criteria can establish a diagnosis of EGPA:(8) • Asthma (a history of wheezing or diffuse high-pitched rales on expiration) • Eosinophilia (greater than 10% eosinophils on white blood cell differential count) • Mononeuropathy (including multiplex), multiple mononeuropathies, or polyneuropathy attributed to a systemic vasculitis • Migratory or transient pulmonary infiltrates detected radiographically • Paranasal sinus abnormality • Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas The Lanham criteria is also used for the diagnosis of EGPA. The Lanham criteria requires the patient to have all three of the following: asthma, peak peripheral blood eosinophilia in excess of 1500 cells/microliter, and systemic vasculitis involving two or more extra-pulmonary organs.(8,9) Glucocorticosteroids are the mainstay of therapy for EGPA, as induction and maintenance therapy. Immunosuppressive therapy (e.g., cyclophosphamide) is used as add on remission induction therapy for patients with life and/or organ manifestations (i.e., heart, GI, central nervous system, alveolar hemorrhage and/or glomerulonephritis).(7,18) The maintenance glucocorticoid dose should be adapted to tightly control each patient's needs to prevent relapses of systemic manifestations and control asthma. Maintenance therapy with azathioprine or methotrexate is recommended for patients with life and/or organ threatening disease manifestations after remission has been achieved. Maintenance therapy with an immunosuppressant can be started 2 -3 weeks after the last cyclophosphamide pulse or a few days after oral cyclophosphamide. Glucocorticoid therapy alone as maintenance therapy maybe suitable for patients without life and/or organ threatening disease manifestations. However, additional immunosuppressants can be considered for select patients when prednisone dose cannot be tapered to less than 7.5 mg/day after 3-4 months of therapy or for patients with recurrent disease. First line immunosuppressants used are azathioprine, methotrexate, and mycophenolate mofetil. Other, second line therapy options are intravenous immune globulin, rituximab, and interferon-alpha.(7,18)

	Nucala Efficacy A total of 136 subjects with EGPA were evaluated in a randomized, placebo-controlled, multicenter, 52-week trial. Subjects enrolled had a diagnosis of EGPA for at least 6 months prior to enrollment with a history of relapsing or refractory disease and were on a stable dosage of oral prednisolone or prednisone of greater than or equal to 7.5 mg/day (but not greater than 50 mg/day) for at least 4 weeks prior to enrollment. Subjects received 300 mg of mepolizumab or placebo administered subcutaneously once every 4 weeks while continuing their stable OCS therapy. Starting at Week 4, OCS was tapered during the treatment period at the discretion of the investigator. The co-primary endpoints were the total accrued duration of remission over the 52-week treatment period, defined as Birmingham Vasculitis Activity Score (BVAS) = 0 (no active vasculitis) plus prednisolone or prednisone dose less than or equal to 4 mg/day, and the proportion of subjects in remission at both Week 36 and Week 48 of treatment. The BVAS is a clinician-completed tool to assess clinically active vasculitis that would likely require treatment, after exclusion of other causes.(1) A significantly higher proportion of subjects receiving mepolizumab achieved remission at both Week 36 and Week 48 compared with placebo. In addition, significantly more subjects receiving mepolizumab achieved remission within the first 24 weeks and remained in remission for the remainder of the 52-week study treatment period compared with placebo (19% for mepolizumab versus 1% for placebo; OR 19.7; 95% CI: 2.3, 167.9).(1) The time to first relapse (defined as worsening related to vasculitis, asthma, or sino-nasal symptoms requiring an increase in dose of corticosteroids or immunosuppressive therapy or hospitalization) was significantly longer for subjects receiving mepolizumab compared with placebo with a hazard ratio of 0.32 (95% CI: 0.21, 0.5). Additionally, subjects receiving mepolizumab had a reduction in rate of relapse compared with subjects receiving placebo (rate ratio 0.50; 95% CI: 0.36, 0.70 for mepolizumab compared with placebo). The incidence and number of relapse types (vasculitis, asthma, sino-nasal) were numerically lower with mepolizumab compared with placebo.(1) Subjects receiving mepolizumab had a significantly greater reduction in average daily OCS dose compared with subjects receiving placebo during Weeks 48 to 52.(1)
Hypereosinophilic Syndrome (HES)	The eosinophilias encompass a broad range of non-hematologic (secondary or reactive) and hematologic (primary or clonal) disorders with potential for end-organ damage.(12) Hypereosinophilia (HE) has generally been defined as peripheral blood eosinophil count greater than 1500 cells/microliter, OR pathologic confirmation of tissue HE by at least one of the following: percentage of eosinophils in bone marrow section exceeds 20% of all nucleated cells, marked deposition of eosinophil granule proteins is found, or tissue infiltration by eosinophils is extensive in the opinion of the pathologist.(11) To establish a diagnosis of HES, all three of the following criteria must be met:(11,12,13) • Criteria for HE fulfilled • Evidence of HE-related organ damage (e.g., fibrosis of lung, heart, digestive tract, skin, etc; thrombosis with or without thromboembolism; cutaneous erythema, edema/angioedema, ulceration, pruritis, or eczema; peripheral or

	central neuropathy with chronic or recurrent neurologic deficit; other organ system involvement such as liver, pancreas, kidney) • Exclusion of secondary (non-hematologic) causes of eosinophilia (e.g., infection, allergy/atopy, medications, collagen vascular disease, metabolic [e.g., adrenal insufficiency], solid tumor/lymphoma) Although the clinical manifestations can be similar irrespective of the cause of the eosinophilia, the choice of the initial therapeutic agent(s) for a given patient depends mainly on whether the patient has clinical features consistent with a myeloid disorder. Patients with myeloid variants of HES (e.g., *PDGFRA*-positive HES) often have an aggressive course with disabling complications and high mortality in the absence of treatment, and are treated initially with imatinib; those with other types of HES are treated with an initial trial of glucocorticoids.(11,12,13,14) Oral corticosteroids have been used for decades in the treatment of HES and, with the exception of imatinib for PDGFRA-associated HES as noted above, remain the first-line treatment for most patients. Hydroxyurea is a typical second-line agent, whether used as monotherapy or in conjunction with corticosteroids. Additional immunomodulatory and cytotoxic agent options include interferon-α, azathioprine, cyclosporine, methotrexate, and tacrolimus.(12,13,14) Despite the wide variety of commercially available immunomodulatory and cytotoxic agents, a significant proportion of patients with HES are treatment-refractory or experience treatment-related toxicity. Monoclonal anti–IL-5 antibody therapy for HES has a number of unique advantages related to the specificity of IL-5 for the eosinophil lineage.(12,13,14) The safety and efficacy of anti–IL-5 therapy mepolizumab, as a corticosteroid-sparing agent in HES, is noted in the section below. **Nucala Efficacy** A total of 108 adult and adolescent patients aged 12 years and older with HES for at least 6 months were evaluated in a randomized, double-blind, placebo-controlled, multicenter, 32-week trial (NCT #02836496). Patients with non-hematologic secondary HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy) or *FIP1L1-PDGFRα* kinase-positive HES were excluded from the trial. Patients received 300 mg of Nucala or placebo subcutaneously once every 4 weeks while continuing their stable HES therapy. Patients entering the trial had experienced at least 2 HES flares within the past 12 months and a blood eosinophil count of 1,000 cells/microliter or higher during screening. Historical HES flares for the trial entry criteria were defined as HES-related worsening of clinical symptoms or blood eosinophil counts requiring an escalation in therapy. Patients must have been on stable background HES therapy for a minimum of 4 weeks prior to randomization; existing HES therapy was maintained throughout the treatment period unless there was symptom worsening that required a dose increase. HES therapy could include chronic or episodic oral corticosteroids (OCS), immunosuppressive, and/or cytotoxic therapy.(1,10) The efficacy of Nucala in HES was established based upon the proportion of patients who experienced a HES flare during the 32-week treatment period. A HES flare was defined as worsening of clinical signs and symptoms of HES or increasing eosinophils (on at least 2 occasions), resulting in the need to increase OCS or increase/add cytotoxic or immunosuppressive HES therapy. Over the 32-week treatment period, the

	incidence of HES flare over the treatment period was 56% for the placebo group and 28% for the group treated with Nucala (50% reduction).(1,10)
Chronic Rhinosinusitis with Nasal Polyposis	Chronic rhinosinusitis with nasal polyposis (CRSwNP) is an inflammatory condition affecting the paranasal sinuses. The International Consensus Statement on allergy and rhinology: Rhinosinusitis indicates that the diagnostic criteria for chronic rhinosinusitis (CRS) consist of ALL the following:(20) • Symptoms greater than or equal to 12 weeks • Two of the following symptoms: o Nasal discharge (rhinorrhea or post-nasal drainage) o Nasal obstruction or congestion o Hyposmia (loss or decreased sense of smell) o Facial pressure or pain • One or more of the following findings: o Evidence of inflammation on nasal endoscopy or computed tomography o Evidence of purulence coming from paranasal sinuses or ostiomeatal complex Sinus computed tomography (CT) and/or nasal endoscopy are needed to determine the presence of sinonasal inflammation and nasal polyps. The exact cause of CRSwNP is unknown, but biopsies of nasal polyps have shown elevated levels of eosinophils.(15) First line therapy for CRSwNP consists of nasal saline irrigation in combination with intranasal corticosteroids.(15,16,17) The American Academy of Family Physicians notes that no one intranasal corticosteroid is superior to another or that increased dosing provides greater effectiveness. The American Academy of Otolaryngology recommends a short course of oral corticosteroids if no response is seen with intranasal corticosteroids after 3-months of appropriate use.(17) Short courses of oral corticosteroids (up to three weeks) can improve sinonasal symptoms and endoscopic findings. Surgical intervention may be required in patients in which medical therapy is ineffective.(15,16) **Nucala Efficacy** A randomized, double-blind, multicenter, placebo-controlled 52-week trial (NCT03085797) evaluated Nucala in patients with CRSwNP. The trial inclusion requirements included adult patients on background intranasal corticosteroids (INCS), with recurrent and symptomatic CRSwNP despite at least 1 surgery for the removal of nasal polyps within the previous 10 years. A total of 407 subjects were randomized to receive either 100 mg Nucala (N=206) or placebo (N=201) every 4 weeks for 52 weeks (13 doses). All study participants received mometasone furoate 400 mcg (intolerant participants received 200mcg) daily along with Nucala or placebo. Participants were not required to have sinus CT scans, but were required to have endoscopic confirmation of diagnosis.(1) The co-primary efficacy endpoints were change from baseline to Week 52 in total endoscopic nasal polyps score (NPS; 0-8 scale) as graded by independent blinded assessors and change from baseline in nasal visual analog scale (VAS; 0-10 scale) during weeks 49 to 52.(1)

	Statistically significant efficacy was observed regarding improvement (decrease) in bilateral endoscopic NPS score at week 52, and nasal obstruction VAS score from weeks 49 to 52. Total endoscopic NPS significantly improved at week 52 from baseline with mepolizumab versus placebo (adjusted difference in medians -0.73, 95% CI -1.11 to -0.34; p less than 0.001) and nasal obstruction VAS score during weeks 49–52 also significantly improved (-3.14, -4.09 to -2.18; p less than 0.001).(1) Treatment with Nucala resulted in significant reduction of systemic corticosteroid use and need for sinonasal surgery versus placebo. The proportion of subjects who required surgery was reduced by 57% (HR of 0.43; 95% CI: 0.25, 0.76). Treatment with Nucala also significantly reduced the need for systemic steroids for nasal polyps versus placebo.(1)
SAFETY	Cinqair (reslizumab) is contraindicated in patients with known hypersensitivity to reslizumab or any of its excipients. It also carries a boxed warning for anaphylaxis. Therapy with reslizumab should be discontinued immediately if a patient experiences anaphylaxis.(2) Fasenra (benralizumab) is contraindicated in those with known hypersensitivity to benralizumab or excipients.(3) Nucala (mepolizumab) is contraindicated in patients with history of hypersensitivity to mepolizumab or excipients in the formulation.(1) Benralizumab, mepolizumab, and reslizumab have not been studied for use in combination with Xolair (omalizumab).

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POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
J2786	Cinqair	reslizumab iv infusion soln	100 MG/10ML	M ; N ; O ; Y	N		
J0517 ; J3490	Fasenra pen	benralizumab subcutaneous soln auto-injector	30 MG/ML	M ; N ; O ; Y	N		
J0517	Fasenra	benralizumab subcutaneous soln prefilled syringe	30 MG/ML	M ; N ; O ; Y	N		
J2182	Nucala	mepolizumab subcutaneous solution auto-injector	100 MG/ML	M ; N ; O ; Y	N		
J2182	Nucala	mepolizumab subcutaneous solution pref syringe	100 MG/ML ; 40 MG/0.4ML	M ; N ; O ; Y	N		
J2182	Nucala	mepolizumab for inj	100 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Fasenra	Benralizumab Subcutaneous Soln Prefilled Syringe 30 MG/ML	30 MG/ML	1	SYRNG	56	Days				
Fasenra pen	Benralizumab Subcutaneous Soln Auto-injector 30 MG/ML	30 MG/ML	1	PEN	56	Days				
Nucala	Mepolizumab For Inj 100 MG	100 MG	3	VIALS	28	Days		Severe eosinophilic asthma and CRSwNP: 1 vial/28 days		
Nucala	Mepolizumab Subcutaneous Solution Auto-injector 100 MG/ML	100 MG/ML	3	SYRNGS	28	Days		Severe eosinophilic asthma and CRSwNP: 1 syringe/28 days		
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe	40 MG/0.4 ML	1	SYRNG	28	Days				
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe 100 MG/ML	100 MG/ML	3	SYRNGS	28	Days		Severe eosinophilic asthma and CRSwNP: 1 syringe/28 days		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Cinqair	reslizumab iv infusion soln	100 MG/10ML	Commercial ; HIM ; ResultsRx
Fasenra	benralizumab subcutaneous soln prefilled syringe	30 MG/ML	Commercial ; HIM ; ResultsRx
Fasenra pen	benralizumab subcutaneous soln auto-injector	30 MG/ML	Commercial ; HIM ; ResultsRx
Nucala	mepolizumab for inj	100 MG	Commercial ; HIM ; ResultsRx
Nucala	mepolizumab subcutaneous solution auto-injector	100 MG/ML	Commercial ; HIM ; ResultsRx
Nucala	mepolizumab subcutaneous solution pref syringe	100 MG/ML ; 40 MG/0.4ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fasenra	Benralizumab Subcutaneous Soln Prefilled Syringe 30 MG/ML	30 MG/ML	Commercial ; HIM ; ResultsRx
Fasenra pen	Benralizumab Subcutaneous Soln Auto-injector 30 MG/ML	30 MG/ML	Commercial ; HIM ; ResultsRx
Nucala	Mepolizumab For Inj 100 MG	100 MG	Commercial ; HIM ; ResultsRx
Nucala	Mepolizumab Subcutaneous Solution Auto-injector 100 MG/ML	100 MG/ML	Commercial ; HIM ; ResultsRx
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe	40 MG/0.4ML	Commercial ; HIM ; ResultsRx
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe 100 MG/ML	100 MG/ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The patient has a diagnosis of severe eosinophilic asthma and ALL of the following:
      1. The patient's diagnosis has been confirmed by ONE of the following:
         A. The patient has a baseline (prior to therapy with the requested agent) blood eosinophilic count of 150 cells/microliter or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR**
         B. The patient has sputum eosinophils 2% or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **AND**
      2. The patient has a history of uncontrolled asthma while on asthma control therapy as demonstrated by ONE of the following:
         A. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months **OR**
         B. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months **OR**
         C. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered **OR**
         D. The patient has baseline (prior to therapy with the requested agent) Forced Expiratory Volume (FEV1) that is less than 80% of predicted **AND**

Module	Clinical Criteria for Approval
	3. ONE of the following: A. The patient is NOT currently being treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months **OR** B. The patient is currently being treated with the requested agent AND ONE of the following: 1. Is currently treated with an inhaled corticosteroid for at least 3 months that is adequately dosed to control symptoms **OR** 2. Is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months **OR** C. The patient has an intolerance or hypersensitivity to inhaled corticosteroid therapy **OR** D. The patient has an FDA labeled contraindication to ALL inhaled corticosteroids **AND** 4. ONE of the following: A. The patient is currently being treated for at least 3 months with ONE of the following: 1. A long-acting beta-2 agonist (LABA) **OR** 2. A leukotriene receptor antagonist (LTRA) **OR** 3. Long-acting muscarinic antagonist (LAMA) **OR** 4. Theophylline **OR** B. The patient has an intolerance or hypersensitivity to therapy with long-acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), long-acting muscarinic antagonists (LAMA), or theophylline **OR** C. The patient has an FDA labeled contraindication to ALL long-acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA), long-acting muscarinic antagonists (LAMA), AND theophylline **AND** 5. The patient will continue asthma control therapy (e.g., ICS, ICS/LABA, LTRA, LAMA, theophylline) in combination with the requested agent **AND** 6. If the requested agent is Cinqair, the patient has a baseline (prior to therapy with the requested agent) blood eosinophil count of 400 cells/microliter or higher **OR** B. The patient has a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) and ALL of the following: 1. The requested agent is Nucala **AND** 2. The patient has had a diagnosis of EGPA for at least 6 months with a history of relapsing or refractory disease **AND** 3. The patient's diagnosis of EGPA was confirmed by ONE of the following: A. The patient meets 4 of the following: 1. Asthma (history of wheezing or diffuse high-pitched rales on expiration) 2. Eosinophilia (greater than 10% eosinophils on white blood cell differential count) 3. Mononeuropathy (including multiplex), multiple mononeuropathies, or polyneuropathy attributed to a systemic vasculitis 4. Migratory or transient pulmonary infiltrates detected radiographically 5. Paranasal sinus abnormality 6. Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas **OR** B. The patient meets ALL of the following: 1. Medical history of asthma **AND** 2. Peak peripheral blood eosinophilia greater than 1500 cells/microliter **AND** 3. Systemic vasculitis involving two or more extra-pulmonary organs **AND** 4. ONE of the following:

Module	Clinical Criteria for Approval
	A. The patient is currently on maximally tolerated oral corticosteroid therapy **OR** B. The patient has an intolerance or hypersensitivity to oral corticosteroid therapy **OR** C. The patient has an FDA labeled contraindication to ALL oral corticosteroids **AND** 5. ONE of the following: A. The patient has tried and had an inadequate response to ONE oral immunosuppressant (i.e., azathioprine, methotrexate, mycophenolate mofetil) **OR** B. The patient has an intolerance or hypersensitivity to oral immunosuppressant therapy **OR** C. The patient has an FDA labeled contraindication to ALL oral immunosuppressants **OR** C. The patient has a diagnosis of hypereosinophilic syndrome (HES) and ALL of the following: 1. The requested agent is Nucala **AND** 2. BOTH of the following: A. The patient has had a diagnosis of HES for at least 6 months **AND** B. The patient has a history of at least 2 HES flares within the past 12 months (i.e., worsening of clinical symptoms and/or blood eosinophil counts requiring an escalation in therapy) **AND** 3. The patient's diagnosis of HES was confirmed by BOTH of the following: A. ONE of the following: 1. The patient has a peripheral blood eosinophil count greater than 1500 cells/microliter **OR** 2. The patient has a percentage of eosinophils in bone marrow section exceeding 20% of all nucleated cells **OR** 3. The patient has marked deposition of eosinophil granule proteins found **OR** 4. The patient has tissue infiltration by eosinophils that is extensive in the opinion of a pathologist **AND** B. ALL of the following: 1. Secondary (reactive, non-hematologic) causes of eosinophilia have been excluded (e.g., infection, allergy/atopy, medications, collagen vascular disease, metabolic [e.g., adrenal insufficiency], solid tumor/lymphoma) **AND** 2. There is evidence of hypereosinophilia-related organ damage (e.g., fibrosis of lung, heart, digestive tract, skin, etc; thrombosis with or without thromboembolism; cutaneous erythema, edema/angioedema, ulceration, pruritis, or eczema; peripheral or central neuropathy with chronic or recurrent neurologic deficit; other organ system involvement such as liver, pancreas, kidney) **AND** 3. The patient does NOT have FIP1L1-PDGFRA-positive disease **AND** 4. ONE of the following: A. The patient is currently being treated with maximally tolerated oral corticosteroid (OCS) **OR** B. The patient has an intolerance or hypersensitivity to oral corticosteroid (OCS) therapy **OR** C. The patient has an FDA labeled contraindication to ALL oral corticosteroids **AND** 5. ONE of the following: A. The patient is currently being treated with ONE of the following: 1. Hydroxyurea **OR** 2. Interferon-α **OR** 3. Another immunosuppressive agent (e.g., azathioprine, cyclosporine, methotrexate, tacrolimus) **OR**

Module	Clinical Criteria for Approval
	B. The patient has an intolerance or hypersensitivity to therapy with hydroxyurea, interferon-α, or immunosuppressive agents (e.g., azathioprine, cyclosporine, methotrexate, tacrolimus) **OR** C. The patient has an FDA labeled contraindication to hydroxyurea, interferon-α, and ALL immunosuppressive agents (e.g., azathioprine, cyclosporine, methotrexate, tacrolimus) **AND** 6. The patient will continue existing HES therapy (e.g., OCS, hydroxyurea, interferon-α, immunosuppressants) in combination with the requested agent **OR** D. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND ALL of the following: 1. The requested agent is Nucala **AND** 2. There is information indicating the patient's diagnosis was confirmed by ONE of the following: A. Anterior rhinoscopy or endoscopy **OR** B. Computed tomography (CT) of the sinuses **AND** 3. ONE of the following: A. ONE of the following: 1. The patient had an inadequate response to sinonasal surgery **OR** 2. The patient is NOT a candidate for sinonasal surgery **OR** B. ONE of the following: 1. The patient has tried and had an inadequate response to oral systemic corticosteroids **OR** 2. The patient has an intolerance or hypersensitivity to therapy with oral systemic corticosteroids **OR** 3. The patient has an FDA labeled contraindication to ALL oral systemic corticosteroids **AND** 4. ONE of the following: A. The patient has tried and had an inadequate response to intranasal corticosteroids (e.g., fluticasone, Sinuva) used for at least a 3-month trial **OR** B. The patient has an intolerance or hypersensitivity to therapy with intranasal corticosteroids (e.g., fluticasone, Sinuva) **OR** C. The patient has an FDA labeled contraindication to ALL intranasal corticosteroids **AND** 5. BOTH of the following: A. The patient is currently treated with standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) **AND** B. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent **OR** E. The patient has another FDA approved indication for the requested agent and route of administration **OR** F. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, otolaryngologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND**

Module	Clinical Criteria for Approval
	2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval**: 6 months for severe eosinophilic asthma; 12 months for EGPA, HES, CRSwNP, and all other FDA approved indications For Fasenra, approve loading dose for new starts and the maintenance dose for the remainder of the 6 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process **AND** 2. ONE of the following: A. The patient has a diagnosis of severe eosinophilic asthma AND BOTH of the following: 1. The patient has had improvements or stabilization with the requested agent from baseline (prior to therapy with the requested agent) as indicated by ONE of the following: A. Increase in percent predicted Forced Expiratory Volume (FEV1) **OR** B. Decrease in the dose of inhaled corticosteroids required to control the patient's asthma **OR** C. Decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma **OR** D. Decrease in number of hospitalizations, need for mechanical ventilation, or visits to urgent care or emergency room due to exacerbations of asthma **AND** 2. The patient is currently treated and is compliant with asthma control therapy [i.e., inhaled corticosteroids (ICS), ICS/long-acting beta-2 agonist (ICS/LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline] **OR** B. The patient has a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) AND ALL of the following: 1. The requested agent is Nucala **AND** 2. The patient has had improvements or stabilization with the requested agent from baseline (prior to therapy with the requested agent) as indicated by ONE of the following: A. Remission achieved with the requested agent **OR** B. Decrease in oral corticosteroid maintenance dose required for control of symptoms related to EGPA **OR** C. Decrease in hospitalization due to symptoms of EGPA **OR** D. Dose of maintenance corticosteroid therapy and/or immunosuppressant therapy was not increased **AND** 3. ONE of the following: A. The patient is currently treated and is compliant with maintenance therapy with oral corticosteroids **OR**

Module	Clinical Criteria for Approval
	B. The patient has an intolerance or hypersensitivity to oral corticosteroid therapy **OR** C. The patient has an FDA labeled contraindication to ALL oral corticosteroids **OR** C. The patient has a diagnosis of hypereosinophilic syndrome (HES) AND ALL of the following: 1. The requested agent is Nucala **AND** 2. The patient has had improvements or stabilization with the requested agent from baseline (prior to therapy with the requested agent) as indicated by ONE of the following: A. Decrease in incidence of HES flares **OR** B. Escalation of therapy (due to HES-related worsening of clinical symptoms or increased blood eosinophil counts) has not been required **AND** 3. ONE of the following: A. The patient is currently treated and is compliant with oral corticosteroid and/or other maintenance therapy (e.g., hydroxyurea, interferon-α, azathioprine, cyclosporine, methotrexate, tacrolimus) **OR** B. The patient has an intolerance or hypersensitivity to therapy with oral corticosteroids or other maintenance agents (e.g., hydroxyurea, interferon-α, azathioprine, cyclosporine, methotrexate, tacrolimus) **OR** C. The patient has an FDA labeled contraindication to ALL oral corticosteroids AND maintenance agents (e.g., hydroxyurea, interferon-α, azathioprine, cyclosporine, methotrexate, tacrolimus) **OR** D. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND ALL of the following: 1. The requested agent is Nucala **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent **OR** E. The patient has another FDA approved indication for the requested agent and route of administration AND has had clinical benefit with the requested agent **OR** F. The patient has another indication that is supported in compendia for the requested agent and route of administration AND has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, otolaryngologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval**: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

Module	Clinical Criteria for Approval

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested agent is subject to quantity limit (i.e., Fasenra, Nucala) AND ONE of the following: A. The quantity (dose) requested does NOT exceed the program quantity limit **OR** B. ALL of the following: 1. The requested quantity (dose) is greater than the program quantity limit **AND** 2. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 3. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 2. The requested agent is NOT subject to quantity limit (i.e., Cinqair) AND the requested quantity (dose) is within FDA labeling for the requested indication **Length of Approval:** Initial: 6 months for severe eosinophilic asthma; 12 months for EGPA, HES, CRSwNP, and all other FDA approved indications For Fasenra, approve loading dose for new starts and the maintenance dose for the remainder of the 6 months Renewal: 12 months

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Adbry (tralokinumab-ldrm) Actemra (tocilizumab) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab)

Contraindicated as Concomitant Therapy
Dupixent (dupilumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Humira (adalimumab)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Nucala (mepolizumab)
Olumiant (baricitinib)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Siliq (brodalumab)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)

Contraindicated as Concomitant Therapy
Sotyktu (deucravacitinib)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Zeposia (ozanimod)

