Interleukin-5 (IL-5) Inhibitors Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date
05-01-2024

Date of Origin
07-01-2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
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 Limitations of use: • Treatment of other eosinophilic conditions • Relief of acute bronchospasm or status asthmaticus		2
Nucala® (mepolizumab) Injection for subcutaneous use	Add-on maintenance treatment of patients aged 6 years and older with severe asthma and with an eosinophilic phenotype 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 greater than or equal to 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 Limitation of use: • Not for relief of acute bronchospasm or status asthmaticus		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.(3,5) It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.(3) 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.(3,5)
	
	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.(5) 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 Step 3 or Step 4 treatment (e.g., low- or medium-dose inhaled corticosteroids [ICS] in combination with a long-acting beta agonist [LABA] in either treatment track). Severe asthma is defined as asthma that remains uncontrolled despite optimized treatment with high-dose ICS-LABA, or that requires high-dose ICS-LABA to prevent it from becoming uncontrolled. Severe asthma must be distinguished from asthma that is difficult to treat due to inadequate or inappropriate treatment, or persistent problems with adherence or comorbidities such as chronic rhinosinusitis or obesity, as they need very different treatment compared with if asthma is relatively refractory to high-dose ICS-LABA or even oral corticosteroids (OCS). 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 2023 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.(5)
	
	2023 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 exacerbations compared with regimens with short-acting β2-agonist (SABA) as reliever, and is a simpler regimen. Note ICS-formoterol should not be used as the reliever by patients taking any other (non-formoterol) ICS-LABA or ICS-LAMA:(5)
	
	• Step 1:
	  ○ As-needed low dose ICS-formoterol
	• Step 2:
	  ○ As-needed low dose ICS-formoterol
	• Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up
	  ○ Maintenance: low dose ICS-formoterol
	  ○ Reliever: as-needed low dose ICS-formoterol
	• Step 4:
	  ○ Maintenance: medium dose ICS-formoterol
	  ○ Reliever: as-needed low dose ICS-formoterol
	• Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment
	  ○ Maintenance: consider high dose ICS-formoterol
	  ○ Reliever: as-needed low dose ICS-formoterol
	  ○ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers
	  ○ Refer for phenotypic assessment +/- biologic therapy
	  ▪ Add-on anti-IgE for severe allergic asthma
	  • SC omalizumab in patients greater than or equal to 6 years
	  ▪ Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma

	• Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age • Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years • Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years ▪ Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma • SC tezepelumab for patients greater than or equal to 12 years o Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance o Maintenance oral corticosteroids (OCS) should be used only as last resort, because short-term and long-term systemic side-effects are common and serious **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 higher risk of exacerbations with SABA-only treatment:(5) • Step 1: o Take ICS whenever SABA taken o Reliever: as-needed ICS-SABA or as needed SABA • Step 2: o Preferred maintenance: low dose ICS o Preferred reliever: as-needed ICS-SABA or as-needed SABA o Alternative options with limited indications, or less evidence for efficacy and/or safety: ▪ Low dose ICS whenever SABA taken ▪ Daily LTRA. These are less effective than daily ICS, particularly for preventing exacerbations and there is a US FDA boxed warning about the risk of serious mental health effects with montelukast ▪ Daily low-dose ICS-LABA as initial therapy leads to faster improvement in symptoms and FEV1 than ICS alone but is costlier, and the reduction in exacerbations compared with SABA is similar to that with ICS ▪ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT) • Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up o Preferred maintenance: low dose ICS-LABA o Preferred reliever: as-needed ICS-SABA or as-needed SABA o Alternative options: ▪ Medium dose ICS ▪ Low-dose ICS plus LTRA but review US FDA boxed warning ▪ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding SLIT • Step 4: o Preferred maintenance: medium/high dose ICS-LABA o Preferred reliever: as-needed ICS-SABA or as-needed SABA o Alternative options: ▪ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium my mist inhaler) • Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium

	▪ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT) • Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment o Maintenance: medium/high dose ICS-LABA o Reliever: as-needed ICS-SABA or as-needed SABA o Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers o Refer for phenotypic assessment +/- biologic therapy ▪ Add-on anti-IgE for severe allergic asthma • SC omalizumab in patients greater than or equal to 6 years ▪ Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma • Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age • Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years • Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years ▪ Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma • SC tezepelumab for patients greater than or equal to 12 years o Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance o Maintenance OCS should only be used as last resort, because short-term and long-term systemic side-effects are common and serious 2023 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:(5) • Step 1: o Low dose ICS taken whenever SABA taken o Reliever: as needed SABA • Step 2: o Preferred: daily low dose ICS o Preferred reliever: as needed SABA o Alternative options: ▪ Low-dose ICS whenever SABA is taken using separate inhalers ▪ Daily LTRA are less effective for exacerbation reduction. Advise parents about US FDA warning on montelukast • Step 3: after checking inhaler technique and adherence, and treating modifiable risk factors (any of the following): o Medium-dose ICS maintenance plus as-needed SABA o Low-dose ICS-LABA maintenance plus as-needed SABA o Maintenance and reliever therapy (MART) with a very low dose of budesonide-formoterol DPI • Step 4: Individual children's responses vary, so each of the Step 3 options may be tried before considering a step-up to Step 4. Refer for expert advice o Preferred: medium dose ICS-LABA plus as-needed SABA o Preferred: low dose ICS-formoterol MART plus as-needed low-dose ICS-formoterol o Alternative options: ▪ Add-on tiotropium ▪ Add-on LTRA • Step 5:

	○ Refer for phenotypic assessment with or without higher dose ICS-LABA ○ Reliever: as needed SABA (or ICS-formoterol reliever for MART) ○ Add on therapy with anti-IgE or anti-IL4R, anti-IL5 ○ As a last resort consider add on low dose OCS but consider side effects **Severe Asthma Phenotype and Eosinophilic Asthma Subphenotype** Roughly 3% to 10% of adults with asthma have severe asthma as defined by the GINA 2023 guidelines.(5) 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:(3,19) • 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).(5) 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:(5) • 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.(5) 2023 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. 2023 GINA recommends the following step-down therapy process in patients responding well to targeted biologic therapy:(5) • 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
Eosinophilic Granulomatosis with Polyangiitis (EGPA)	Eosinophilic granulomatosis with polyangiitis (EGPA), formally known as Churg-Strauss Syndrome, is a rare small-vessel vasculitis that occurs in patients with asthma and eosinophilia and is histologically characterized by tissue eosinophilia, necrotizing vasculitis and eosinophil-rich granulomatous inflammation. EGPA is an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, characterized by asthma, eosinophilia and granulomatous or vasculitic involvement of several organs. Current practice relies on recommendations and guidelines addressing the management of ANCA-associated vasculitis and not specifically developed for EGPA.(20) The main clinical features of EGPA are late-onset allergic rhinitis and asthma, increased blood eosinophil count, and vasculitis manifestations, some of which can be life threatening. 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.(6) The clinical phenotype of EGPA is quite heterogeneous and the diagnosis is not always straightforward. Anti-neutrophil cytoplasmic antibodies (ANCA), usually against myeloperoxidase (MPO), are detectable in approximately 40% of the cases and are associated with a different frequency of clinical manifestations: features of vasculitis, particularly glomerulonephritis, peripheral neuropathy and purpura, occur more often in ANCA-positive patients, whereas the so-called eosinophilic features such as cardiac involvement and gastroenteritis are more frequent in ANCA-negative patients.(20) 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:(7) • 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.(7,8)

The American College of Rheumatology/European Alliance of Associations for Rheumatology developed classification criteria for EGPA broken into clinical criteria as well as laboratory and biopsy criteria. Considerations when applying these criteria(20)

- These classification criteria should be applied to classify a patient as having EGPA when a diagnosis of small- or medium-vessel vasculitis has been made
- Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria

	points
Clinical Criteria	
Obstructive airway disease	+3
Nasal Polyps	+3
Mononeuritis multiplex	+1
Laboratory and Biopsy Criteria	
Blood eosinophil count greater than or equal to 1 X 10^9/liter	+5
Extravascular eosinophilic-predominant inflammation on biopsy	+2
Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA)	-3
Hematuria	-1

Sum the scores for the 7 items, if present. A score of greater than or equal to 6 is needed for classification of EGPA

The Five-Factor Score (FFS) predicts the risk of mortality in patients with an established diagnosis of EGPA, as well as polyarteritis nodosa microscopic polyangiitis or GPA. It includes five factors associated with shortened overall survival, namely, renal insufficiency (serum creatinine > 1.58 mg/dl), proteinuria > 1 g per day, cardiomyopathy, gastrointestinal involvement and central nervous system (CNS) involvement. The FFS considers clinical manifestations only at the time of diagnosis, the appearance of new manifestations during follow-up should also be taken into account when choosing remission-induction regimens for disease flares. New-onset active EGPA is considered severe if FFS is greater than or equal to 1 or there is presence of peripheral neuropathy, alveolar hemorrhage or other organ-or life-threatening manifestations. For relapsing EGPA severe disease consists of severe systemic relapse and non-severe is respiratory relapse alone or non-severe systemic relapse.(20)

For remission induction in patients with new-onset, active EGPA, glucocorticoids should be administered as initial therapy. In patients with severe disease cyclophosphamide or rituximab and/or disease modifying anti-rheumatic drugs (DMARDs) should be added to glucocorticoid therapy. Remission maintenance for non-severe disease guidelines recommend glucocorticoids plus mepolizumab. Remission maintenance for severe disease guidelines recommend glucocorticoids plus rituximab and/or mepolizumab and or DMARDs. Although the evidence supporting the use of traditional

	immunosuppressants for remission maintenance in non-severe EGPAS is scarce, these agents are often used in routine clinical practice.(20) Treatment for relapsing EGPA in non-severe disease glucocorticoids alone or glucocorticoids plus mepolizumab along with optimization of inhaled therapies. Treatment of relapsing severe disease high-dose oral glucocorticoids plus cyclophosphamide or rituximab is recommended.(20) Refractory EGPA is defined as unchanged or increased disease activity after 4 weeks of appropriate remission-induction therapy. The persistence or worsening of systemic manifestations should be distinguished from that of respiratory manifestations. Mepolizumab in combination with glucocorticoids is recommended to induce remission in patients with relapsing-refractory EGPA without organ-or life-threatening manifestations. Mepolizumab can also be used for remission maintenance, particularly in patients requiring a daily prednisone greater than or equal to 7.5 mg for the control of their respiratory manifestations.(20)
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. 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.(12) 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)
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:(18)

	• Symptoms greater than or equal to 12 weeks
	• Two of the following symptoms:
	  ○ Nasal discharge (rhinorrhea or post-nasal drainage)
	  ○ Nasal obstruction or congestion
	  ○ Hyposmia (loss or decreased sense of smell)
	  ○ Facial pressure or pain
	• One or more of the following findings:
	  ○ Evidence of inflammation on nasal endoscopy or computed tomography
	  ○ 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)

Efficacy	**Asthma** **Fasenra** 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.(2) 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).(2) **Nucala** 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) **EGPA** **Nucala** 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)

HES

Nucala

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)

CRSwNP

Nucala

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	• Fasenra (benralizumab) is contraindicated in those with known hypersensitivity to benralizumab or excipients.(2) • Nucala (mepolizumab) is contraindicated in patients with history of hypersensitivity to mepolizumab or excipients in the formulation.(1) Benralizumab and mepolizumab have not been studied for use in combination with Xolair (omalizumab).

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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Fasenra pen	benralizumab subcutaneous soln auto-injector	30 MG/ML	M ; N ; O ; Y	N		
Nucala	mepolizumab subcutaneous solution auto-injector	100 MG/ML	M ; N ; O ; Y	N		
Nucala	mepolizumab subcutaneous solution pref syringe	100 MG/ML ; 40 MG/0.4ML	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
Fasenra pen	Benralizumab Subcutaneous Soln Auto-injector 30 MG/ML	30 MG/ML	1	Pen	56	DAYS			
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe	40 MG/0.4 ML	1	Syringe	28	DAYS			

ADDITIONAL QUANTITY LIMIT INFORMATION

Wildcard	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Additional QL Information	Targeted NDCs When Exclusions Exist	Effective Date	Term Date
4460405500D530	Nucala	Mepolizumab Subcutaneous Solution Auto-injector 100 MG/ML	100 MG/ML	Severe eosinophilic asthma and CRSwNP: 1 syringe/28 days. EGPA and HES: 3 syringes/28 days.			
4460405500E530	Nucala	Mepolizumab Subcutaneous Solution Pref Syringe 100 MG/ML	100 MG/ML	Severe eosinophilic asthma and CRSwNP: 1 syringe/28 days. EGPA and HES: 3 syringes/28 days.			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fasenra pen	benralizumab subcutaneous soln auto-injector	30 MG/ML	Medicaid
Nucala	mepolizumab subcutaneous solution auto-injector	100 MG/ML	Medicaid
Nucala	mepolizumab subcutaneous solution pref syringe	100 MG/ML ; 40 MG/0.4ML	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fasenra pen	Benralizumab Subcutaneous Soln Auto-injector 30 MG/ML	30 MG/ML	Medicaid
Nucala	Mepolizumab Subcutaneous Solution Auto-injector 100 MG/ML	100 MG/ML	Medicaid
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe	40 MG/0.4ML	Medicaid
Nucala	Mepolizumab Subcutaneous Solution Pref Syringe 100 MG/ML	100 MG/ML	Medicaid

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 a fraction of exhaled nitric oxide (FeNO) of 20 parts per billion or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR** C. 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** 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 **OR** B. The patient is currently being treated with the requested agent AND ONE of the following:

Module	Clinical Criteria for Approval
	1. Is currently treated with an inhaled corticosteroid that is adequately dosed to control symptoms **OR** 2. Is currently treated with a maximally tolerated inhaled corticosteroid **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 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) AND long-acting muscarinic antagonists (LAMA) **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 Nucala, then ONE of the following: A. The patient's medication history includes use of Fasenra AND ONE of the following: 1. The patient has had an inadequate response to Fasenra **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over Fasenra **OR** B. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Fasenra **OR** C. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** D. The prescriber has provided documentation that Fasenra cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **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

Module	Clinical Criteria for Approval
	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: 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 **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL oral corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 5. ONE of the following: A. The patient's medication history includes use of an non-corticosteroid immunosuppressant (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate mofetil, rituximab) AND ONE of the following: 1. The patient has had an inadequate response to ONE non-corticosteroid immunosuppressant (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate mofetil, rituximab) **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over non-corticosteroid immunosuppressant therapy **OR** B. The patient has an intolerance or hypersensitivity to ONE non-corticosteroid immunosuppressant therapy **OR** C. The patient has an FDA labeled contraindication to ALL of the following immunosuppressants: 1. Azathioprine 2. Cyclophosphamide 3. Methotrexate 4. Mycophenolate mofetil **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**

Module	Clinical Criteria for Approval
	3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that azathioprine, cyclophosphamide, methotrexate, AND mycophenolate mofetil cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **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 1000 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 has been evaluation of hypereosinophilia-related organ involvement (e.g., fibrosis of lung, heart, digestive tract, skin; 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 **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL oral corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain

Module	Clinical Criteria for Approval
	reasonable functional ability in performing daily activities or cause physical or mental harm **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** 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) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that hydroxyurea, interferon-α, and ALL immunosuppressive agents (e.g., azathioprine, cyclosporine, methotrexate, tacrolimus) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **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. The patient has at least TWO of the following symptoms consistent with chronic rhinosinusitis (CRS): A. Nasal discharge (rhinorrhea or post-nasal drainage) B. Nasal obstruction or congestion C. Loss or decreased sense of smell (hyposmia) D. Facial pressure or pain **AND** 3. The patient has had symptoms consistent with chronic rhinosinusitis (CRS) for at least 12 consecutive weeks **AND** 4. 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** 5. 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** 6. ONE of the following:

Module	Clinical Criteria for Approval
	A. The patient has tried and had an inadequate response to intranasal corticosteroids (e.g., fluticasone, Sinuva) **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** 7. 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. If the patient has an FDA approved indication, then 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** 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:** CMS Approved Compendia **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: If Quantity Limit applies, please refer to Quantity Limit Criteria. **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 Prior Authorization process **AND** 2. ONE of the following: A. The patient has a diagnosis of severe eosinophilic asthma AND BOTH of the following:

Module	Clinical Criteria for Approval
	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 (FEV_1) **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 (e.g., 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** 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** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL oral corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **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:

Module	Clinical Criteria for Approval
	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 is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL oral corticosteroids and other maintenance agents (e.g., hydroxyurea, interferon-α, azathioprine, cyclosporine, methotrexate, tacrolimus) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **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:** CMS Approved Compendia

Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

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 quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **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 Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab) Cyltezo (adalimumab-adbm)

Contraindicated as Concomitant Therapy
Dupixent (dupilumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Litfulo (ritlecitinib)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)

Contraindicated as Concomitant Therapy
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Siliq (brodalumab)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Velsipity (etrasimod)
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zeposia (ozanimod)
Zymfentra (infliximab-dyyb)