Medicare Part B - Interleukin-5 (IL-5) Inhibitors Prior Authorization Criteria

FDA APPROVED INDICATIONS AND DOSAGE[1-3]

Agent(s)	Indication(s)^	Dosage
Cinqair® (reslizumab)	Add-on maintenance treatment of patients with severe asthma aged 18 years and older with an eosinophilic phenotype*	3 mg/kg once every 4 weeks by intravenous infusion
Fasenra® (benralizumab)	Add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype*	30 mg administered once every 4 weeks for the first 3 doses, then once every 8 weeks thereafter by SC injection into the upper arm, thigh, or abdomen
Nucala® (mepolizumab)	Add-on maintenance treatment of patients aged 6 years and older with severe asthma and with an eosinophilic phenotype~	6-11 years: 40 mg SC once every 4 weeks into the upper arm, thigh, or abdomen 12 years and over: 100 mg SC once every 4 weeks into the upper arm, thigh, or abdomen
	Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA)	300 mg administered once every 4 weeks by SC injection as 3 separate 100 mg injections into the upper arm, thigh, or abdomen
	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	300 mg administered once every 4 weeks by SC injection as 3 separate 100 mg injections into the upper arm, thigh, or abdomen
	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	100 mg administered once every 4 weeks by SC injection into the upper arm, thigh, or abdomen

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

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. In addition, differential diagnosis of asthma should be considered.[4,6]

The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma.[6] 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 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 2021 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]

2021 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations. 2021 GINA guidelines have been updated to include two treatment "tracks", with the key difference being the medication that is used for symptoms relief: as-needed low dose ICS-formoterol in Track 1, and as-needed SABA in Track 2.[6]

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]

- Steps 1 and 2: As-needed low dose ICS-formoterol
    - Alternative options: Daily leukotriene receptor antagonist (LTRA), or add house dust mite (HDM) sublingual immunotherapy (SLIT)
- Step 3: 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 consideration of anti-IgE, anti-IL5/5R, anti-IL4R; consider high dose ICS-formoterol
    - 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, as 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
- Step 3: 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 consideration of anti-IgE, anti-IL5/5R, anti-IL4R; consider high dose ICS-LABA
  - Reliever: As-needed SABA
  - Alternative options: Add azithromycin (adults) or LTRA; add low dose oral corticosteroids (OCS) but consider side effects

2021 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:[6]

- Step 1:
  - Possible controller: as needed ICS taken at the same time as a SABA OR regular low dose ICS with as needed SABA (likelihood of poor adherence should be taken into account)
- Step 2:
  - Preferred controller: daily low dose ICS with as needed SABA
  - 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)
  - Preferred controller:
    - Daily medium dose ICS with as-needed SABA as reliever, or
    - Change to a combination low dose ICS-LABA plus as-needed SABA, or
    - Maintenance and reliever therapy (MART) with very low dose ICS-formoterol
- Step 4:
  - Medium dose ICS-LABA, or
  - MART with low dose budesonide-formoterol
  - Alternative options: high dose ICS-LABA; add-on tiotropium
- Step 5:
  - Refer for expert assessment and advice if not controlled on a moderate dose ICS
  - Alternative options: add-on tiotropium

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) mirror the GINA definition of severe asthma, and define uncontrolled asthma as:[4]

- 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:

- 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]

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.[2]

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. 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. 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. Hallmarks of the disease consist of at least two out of four cardinal symptoms (i.e., facial pain/pressure, hyposmia/anosmia, nasal drainage, and nasal obstruction) for at least 12 consecutive weeks in addition to nasal polyps and sinonasal inflammation.[15,16,17] 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]

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Document History
Original Prime Standard Part B criteria, to be approved by P&T UM Committee 06/2021
Annual Review Prime Standard Part B criteria, with changes to criteria, approved by P&T UM Committee 12/2021

Medicare Part B - Interleukin-5 (IL-5) Inhibitors Prior Authorization Criteria

Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
Cinqair® (reslizumab) **Fasenra®** (benralizumab) **Nucala®** (mepolizumab)	For severe asthma aged 18 years and older with an eosinophilic phenotype: • For all other indications: • None

Brand (generic)	GPI	Multisource Code	HCPCS Code
Cinqair (reslizumab)			
100 mg/10mL vial	44604460002020	M, N, O, or Y	J2786
Fasenra (benralizumab)			
30 mg/mL prefilled syringe	4460402000E520	M, N, O, or Y	J0517
30 mg/mL auto-injector pen	4460402000D520	M, N, O, or Y	J0517
Nucala (mepolizumab)			
100 mg vial	44604055002120	M, N, O, or Y	J2182
100 mg/mL auto-injector	4460405500D530	M, N, O, or Y	J2182
100 mg/mL prefilled syringe	4460405500E530	M, N, O, or Y	J2182

CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents for the requested indication, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)

OR

d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)

OR

e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

AND

3. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months