Medical Necessity Guidelines

Medical Benefit Drugs

Respiratory Interleukins Skilled-administration: Cinqair® (reslizumab), Fasenra® (benralizumab), Nucala® (mepolizumab), Exdensur (depemokimab)

Effective: July 1, 2026

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Public Plans Products

☒ Tufts Health One Care* – A Medicare-Medicaid Plan (a dual-eligible product); Fax 617-673-0956

*The MNG applies to Tufts Health One Care members unless a less restrictive LCD or NCD exists.

Senior Products

☒ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956

☒ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956

☒ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

The majority of patients can manage their asthma symptoms with a combination of inhaled corticosteroids (ICS) and long-acting beta agonists (LABAs), although a subset of patients remain uncontrolled. Researchers have now developed targeted therapies that yield better outcomes in specific patient types. IgE is central to the development of diseases associated with immediate hypersensitivity reactions, such as allergic asthma. In allergic asthma, IgE production occurs within the bronchial and nasal mucosa, with additional production in the lymphoid tissues and bone marrow. IgE binds to receptors resulting in mast cell release and release of other mediators that contribute to bronchoconstriction and airway inflammation. The anti-interleukin-5 agents respiratory interleukins are a recommended add-on biologic therapy option for patients with uncontrolled severe asthma despite optimized maximal therapy. Patient features and medication administration features will guide the selection of the specific respiratory interleukin product.

Treatment guidelines recommend for adults with non-severe eosinophilic granulomatosis with polyangiitis (EGPA) adding Nucala or Fasenra to systemic glucocorticoids. Approval of Nucala in eosinophilic granulomatosis with polyangiitis (EGPA) was based on a multicenter trial of 136 patients with relapsing or refractory EGPA. Treatment with Nucala led to significantly more accrued weeks of remission compared to treatment with placebo, and a higher percentage of participants in remission at weeks 36 and 48. Overall, 44 percent of Nucala-treated patients were able to taper steroids to 4 mg/day or less, compared to 7 percent of placebo-treated patients. However, 47 percent of participants in the mepolizumab group did not achieve remission. Approval of Fasenra in EGPA was based on a noninferiority trial of 140 patients with EGPA, asthma, eosinophilia, and a history of relapsing or refractory disease treated with background prednisolone/prednisone with or without immunosuppressive therapy. Patients were randomized to either Fasenra or Nucala in addition to continued background therapy. At 36 and 48 weeks, treatment with Fasenra demonstrated noninferiority to Nucala for the primary endpoint of remission and the components of remission.

Evidence demonstrates that Nucala can be beneficial in glucocorticoid-sensitive hypereosinophilic syndrome, including idiopathic hypereosinophilic syndrome, lymphocytic variants of hypereosinophilic syndrome, and hypereosinophilic syndrome / EGPA overlap. Approval of Nucala in hypereosinophilic syndrome was based on a multicenter, placebo-controlled, phase 3 trial of 108 patients with hypereosinophilic syndrome. Patients with non-hematologic secondary HES or FIP1L1::PDGFRA-positive hypereosinophilic syndrome were excluded. Patients with at least two disease flares in the past 12 months and a baseline absolute eosinophil count of at least 1000/microliter were included. Compared to placebo, Nucala was associated with a lower percentage of patients experiencing a subsequent disease flare (28% versus 56%). Nucala was also associated with a 66% reduction in the annualized flare rate and in risk of experiencing a flare. Similar proportions of patients in the Nucala and placebo treatment groups experienced on-treatment adverse events (89% versus 87%).

Chronic rhinosinusitis guidelines suggest offering respiratory biologic therapy for patients who have previously undergone functional endoscopic sinus surgery with recurrence of disease following surgery. Evidence demonstrates that Nucala improves

nasal congestion, overall quality of life, and NPS for patients with chronic rhinosinusitis with nasal polyps (CRSwNP). Approval of Nucala for CRSwNP was based on the SYNAPSE trial in which patients with recurrent, severe bilateral nasal polyps and history of one prior functional endoscopic sinus surgery in the past 10 years was included. Patients received Nucala or placebo in addition to standard-of-care saline nasal irrigations and intranasal corticosteroids. Nucala-treated patients had decreased nasal polyps score and nasal obstruction visual analog scale score compared to placebo-treated patients. However, sense of smell did not improve in Nucala-treated patients.

Approval for COPD was based on the Phase 3 MATINEE and METREX trials, which both showed a statistically significant reduction in annualized rate of moderate or severe exacerbations with Nucala versus placebo in patients with COPD and an eosinophilic phenotype when added to triple-inhaled therapy (MATINEE: P = 0.01; METREX: P = 0.04). Incidence of adverse events was similar between Nucala and placebo groups.

Fasenra's HES approval was based on positive results from the NATRON Phase III trial that evaluated the efficacy and safety of Fasenra in patients with HES.[1,2] In the trial, treatment with Fasenra delayed the time to first HES flare and significantly reduced the risk of first HES flare compared to placebo by 65%

The approval for Exdensur was supported by results from the Phase 3 SWIFT-1 and SWIFT-2 trials. In these studies, patients who received Exdensur had a significant reduction (58% and 48%, respectively) in the rate of annualized asthma exacerbations over 52 weeks with two doses/year versus placebo; both groups also received standard of care.

Food and Drug Administration (FDA) Approved Indications:

Cinqair (reslizumab) is an interleukin-5 antagonist monoclonal antibody (IgG4 kappa) indicated for:

- **Maintenance treatment of severe asthma**
  Add-on maintenance treatment of patients with severe asthma aged 18 years and older and with an eosinophilic phenotype. Cinqair (reslizumab) is not indicated for treatment of other eosinophilic conditions or for relief of acute bronchospasm or status asthmaticus.

Fasenra (benralizumab) is an interleukin-5 alpha directed cytolytic monoclonal antibody (IgG1, kappa) indicated for:

- **Eosinophilic granulomatosis with polyangiitis**
  The treatment of adult patients with eosinophilic granulomatosis with polyangiitis
- **Maintenance treatment of severe asthma**
  Add-on maintenance treatment of adult and pediatric patients aged 6 years and older and with severe asthma, and with an eosinophilic phenotype. Fasenra (benralizumab) is not indicated for treatment of other eosinophilic conditions or for relief of acute bronchospasm or status asthmaticus.
- **Hypereosinophilic Syndrome**
  The treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome without an identifiable non-hematologic secondary cause

Nucala (mepolizumab) is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) indicated for:

- **Eosinophilic granulomatosis with polyangiitis**
  The treatment of adult patients with eosinophilic granulomatosis with polyangiitis
- **Hypereosinophilic Syndrome**
  The treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome for at least 6 months without an identifiable non-hematologic secondary cause
- **Maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP)**
  Add-on maintenance treatment of CRSwNP in adult patients 18 years of age and older with Inadequate response to nasal corticosteroids
- **Maintenance treatment of severe asthma**
  Add-on maintenance treatment of patients with severe asthma aged 6 years and older, and with an eosinophilic phenotype. Nucala (mepolizumab) is not indicated for the relief of acute bronchospasm or status asthmaticus
- **COPD**
  Add-on maintenance treatment for adult patients with inadequately controlled chronic obstructive pulmonary disease (COPD) and an eosinophilic phenotype

Exdensur

- **Maintenance treatment of severe asthma**
  Add-on maintenance treatment of adult and pediatric patients aged 12 years and older and with severe asthma, and with an eosinophilic phenotype

Clinical Guideline Coverage Criteria

The plan may authorize coverage of a Respiratory Interleukin Skilled-administration product for Members when the following criteria are met:

Cinqair

1. Documented diagnosis of severe asthma with an eosinophilic phenotype

AND

2. Documentation the requested medication is being prescribed as add-on maintenance treatment

AND

3. Patient is 18 years of age or older

Fasenra

1. Documented of all of the following:
    a. Diagnosis of severe asthma with an eosinophilic phenotype
    b. The requested medication is being prescribed as add-on maintenance treatment
    c. Patient is 6 years of age or older

OR

2. Documentation of all of the following:
    a. Diagnosis of eosinophilic granulomatosis with polyangiitis
    b. Patient is 18 years of age or older

OR

3. Documentation of all of the following:
    a. Diagnosis hypereosinophilic syndrome without an identifiable non-hematologic secondary cause
    b. Patient is 12 years of age or older

Nucala

1. Documentation of both of the following:
    a. Diagnosis of eosinophilic granulomatosis with polyangiitis
    b. Patient is 18 years of age or older

OR

2. Documentation of both of the following:
    a. Diagnosis hypereosinophilic syndrome for at least 6 months without an identifiable non-hematologic secondary cause
    b. Patient is 12 years of age or older

OR

3. Documentation of all of the following:
    a. Diagnosis of chronic rhinosinusitis with nasal polyps
    b. Patient is 18 years of age or older
    c. Requested medication is being prescribed as add-on maintenance treatment
    d. Inadequate response to nasal corticosteroids

OR

4. Documentation of all of the following:
    a. Diagnosis of severe asthma with an eosinophilic phenotype
    b. Patient is 6 years of age or older
    c. Requested medication is being prescribed as add-on maintenance treatment

OR

5. Documentation of all of the following:
    a. Diagnosis of COPD confirmed by postbronchodilator FEV1/FVC <0.7 on spirometry
    b. Blood eosinophil count ≥150 cells/μL in the previous 12 months
    c. A history of ≥2 moderate or ≥1 severe COPD exacerbations within the last year despite the adherent use of inhaled LABA, LAMA, and ICS triple therapy
        i. Moderate exacerbation is defined as requiring treatment with either systemic corticosteroids and/or antibiotics
        ii. Severe exacerbation is defined as requiring hospitalization.
    d. Patient is not receiving Nucala in combination with Dupixent or Ohtuvayre
    e. Prescribed by or in consultation with a pulmonologist

Exdensur

Initial authorization

1. Submission of medical charts documenting a diagnosis of severe asthma with a pre-treatment peripheral blood eosinophil level greater than or equal to 150 cells per microliter
2. Documentation of history of failure to a minimum three (3) month trial with a maximally tolerated inhaled corticosteroid plus at least one other asthma maintenance medication (e.g., long-acting inhaled beta2-agonist, long-acting muscarinic antagonist, leukotriene receptor antagonist), unless contraindicated
3. Documentation the requested medication will be used as add-on maintenance therapy with a maximally tolerated inhaled corticosteroid plus at least one other asthma maintenance medication (e.g., long-acting inhaled beta2-agonist, long-acting muscarinic antagonist, leukotriene receptor antagonist), unless contraindicated)
4. Two or more asthma exacerbations requiring systemic corticosteroid treatment or one asthma exacerbation resulting in hospitalization in the past 12 months
5. Documented trial and failure with omalizumab
6. Patient is not receiving Exdensur in combination with another biologic medication indicated for asthma treatment
7. Prescribed by or in consultation with an allergist, immunologist, or pulmonologist

Reauthorization

1. Documented diagnosis of severe asthma of eosinophilic phenotype
2. Prescribed by or in consultation with an allergist, immunologist, or pulmonologist
3. Submission of medical charts documenting the patient has experienced a therapeutic response as defined by at least **one (1)** of the following:
   a. Increase in percent Forced Expiratory Volume (FEV1) from pretreatment baseline
   b. Reduction in the dose of inhaled corticosteroids required to control asthma
   c. Reduction in asthma exacerbations (e.g., decreased frequency of use of unscheduled emergency department/urgent care visits/hospitalizations)
   d. Reduction in asthma symptoms (e.g., chest tightness, coughing, shortness of breath, or nocturnal awakenings)
   e. Reduction in the use of oral corticosteroids to treat and/or prevent asthma exacerbations
4. Patient is not receiving Exdensur in combination with another biologic medication indicated for asthma treatment

Limitations

Initial and reauthorization determinations for Exdensur will be approved for 12 months

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J0517	Injection, benralizumab, 1 mg
J2182	Injection, mepolizumab, 1 mg
J2786	Injection, reslizumab, 1 mg
J0517	Injection, depemokimab-ulaa, 1 mg

References

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Approval And Revision History

September 13, 2022: Reviewed by Pharmacy and Therapeutics Committee (P&T).

Subsequent endorsement date(s) and changes made:

- September 21, 2022: Reviewed by the Medical Policy Approval Committee (MPAC).
- December 12, 2024: Updated title of Medical Necessity Guideline from Nucala to Respiratory Interleukins Skilled-administration. Added Cinqair and Fasenra to the Medical Necessity Guideline. Added requirements for use as add-on treatment throughout the Medical Necessity Guideline in line with package labeling. Added the requirement for an inadequate response to an intranasal corticosteroids for chronic rhinosinusitis with nasal polyps. Removed Limitations The Plan may authorize coverage of Nucala (mepolizumab) for up to 12 months when coverage criteria are met and All other indications are considered experimental/investigational and not medically necessary. Administrative Update in support of calendar year 2024 Medicare Advantage and PDP Final Rule (eff 3/1/24).
- December 2023: Administrative update to rebrand Tufts Health Unify to Tufts Health One Care for 2024.
- November 12, 2024: Updated age requirements for Fasenra for asthma to patients at least 6 years of age based on the expanded indication. Added coverage criteria for Fasenra's supplemental indication for EGPA (eff 1/1/25).
- December 2024: Joint Medical Policy and Health Care Services UM Committee review (eff 1/1/25).
- July 2025: Administrative update to remove Harvard Pilgrim Health Care Stride Medicare Advantage from the Medical Necessity Guideline template.
- December 8, 2025: Added COPD indication for Nucala (effective 1/1/26)
- December 2025: Joint Medical Policy and Health Care Services UM Committee review (effective 1/1/26)
- June 2026: Joint Medical Policy and Health Care Services UM Committee review; added HES indication to criteria for Fasenra; added Exdensur and associated criteria to the MNG (effective 7/1/26)

Background, Product and Disclaimer Information

Point32Health prior authorization criteria to be applied to Medicare Advantage plan members is based on guidance from Medicare laws, National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs). When no guidance is provided, Point32Health uses clinical practice guidance published by relevant medical societies, relevant medical literature, Food and Drug Administration (FDA)-approved package labeling, and drug compendia to develop prior authorization criteria to apply to Medicare Advantage plan members. Medications that require prior authorization generally meet one or more of the

following criteria: Drug product has the potential to be used for cosmetic purposes; drug product is not considered as first-line treatment by medically accepted practice guidelines, evidence to support the safety and efficacy of a drug product is poor, or drug product has the potential to be used for indications outside of the indications approved by the FDA. Prior authorization and use of the coverage criteria within this Medical Necessity Guideline will ensure drug therapy is medically necessary, clinically appropriate, and aligns with evidence-based guidelines. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests revisions.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic