Pharmacy Medical Necessity Guidelines: Respiratory Interleukins: Cinqair® (reslizumab), Fasenra™ (benralizumab), Nucala® (mepolizumab)

Effective: January 1, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	MED /RX	Department to Review	PRECERT /MM / RXUM

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☒ Tufts Health Plan Commercial products – large group plans
☒ Tufts Health Plan Commercial products – small group and individual plans
☒ Tufts Health Freedom Plan products – large group plans
☒ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☐ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:

Cinqair, Fasenra, Nucala vials:
All plans except Tufts Health Public Plans:
PRECERT: 617.972.9409

Tufts Health Public Plans only:
MM: 888.415.9055

Fasenra and Nucala pre-filled autoinjector and/or syringe
RXUM: 617.673.0988

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-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:

- **Maintenance treatment of severe asthma**
  Add-on maintenance treatment of patients with severe asthma aged 12 years and older 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.

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 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

COVERAGE GUIDELINES

The plan may authorize coverage of respiratory interleukins for Members when all of the following criteria are met:

Severe Asthma

Initial Therapy

1. Documentation of one of the following:
    a. Pre-treatment serum eosinophil count of at least 400 cells/mcL for Cinqair
    b. Pre-treatment serum eosinophil count of at least 150 cells/mcL for Fasenra or Nucala

AND

2. Member age is at least one of the following
    a. 18 years for Cinqair
    b. 12 years for Fasenra
    c. 6 years for Nucala

AND

3. Prescribed by or in consultation with an asthma specialist (e.g., allergist, immunologist, pulmonologist)

AND

4. Documentation the underlying conditions or triggers for asthma or pulmonary disease are being maximally managed

AND

5. Documentation of poor asthma control or recurrent exacerbations requiring additional treatment despite an adherent trial of at least 3 months duration of a high-dose inhaled corticosteroids (ICS) in combination with a long-acting inhaled beta-2 agonist (LABA), leukotriene modifier or theophylline or the Member is intolerant or has a contraindication to all of these medications

    Note: *Poor asthma control may include but is not limited to clinical documentation of limitation in activities of daily living, nighttime awakening, or dyspnea*
    Note: *Recurrent exacerbation is defined as 2 or more acute exacerbations in a 12-month period*
    Note: *Additional medical treatment may include any of the following: Treatment with oral corticosteroids, emergency department visits, hospitalizations, or frequency office visits*

Reauthorization Criteria

1. Documentation of eosinophilic asthma

AND

2. Member age is at least one of the following:
    a. 18 years for Cinqair
    b. 12 years for Fasenra
    c. 6 years for Nucala

AND

3. Prescribed by or in consultation with an asthma specialist (e.g., allergist, immunologist, pulmonologist)

AND

4. Documentation the Member has experienced a therapeutic response as defined by at least one 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)
    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

The plan may authorize coverage of **Nucala (mepolizumab)** for Members when all of the following criteria are met:

Eosinophilic Granulomatosis with Polyangiitis

Initial Therapy

1. The Member has a documented diagnosis of eosinophilic granulomatosis with polyangiitis based on the presence of 4 or more of the following diagnostic criteria:
    a. Asthma
    b. Eosinophilia (at least 10% eosinophils on the differential leukocyte count)
    c. Mononeuropathy or polyneuropathy
    d. Migratory or transient pulmonary infiltrates on chest x-rays
    e. Paranasal sinus abnormalities
    f. Biopsy containing a blood vessel with extravascular eosinophils

AND

2. Member is at least 18 years of age

AND

3. Prescribed by or in consultation with an asthma specialist (e.g., allergist, immunologist, pulmonologist) or rheumatologist

AND

4. Documentation the Member is stable on corticosteroids or the prescriber has indicated clinical inappropriateness of corticosteroid therapy

AND

5. Documentation of severe disease (e.g., vasculitis with cerebral, cardiac, renal, or gastrointestinal involvement) or disease flares with tapering of corticosteroid therapy

AND

6. Documented trial and failure of, contraindication to, or clinical inappropriateness with treatment with at least one of the following immunosuppressants: azathioprine, cyclophosphamide, or methotrexate

Reauthorization Criteria

1. Documented diagnosis of eosinophilic granulomatosis with polyangiitis

AND

2. Member is at least 18 years of age

AND

3. Prescribed by or in consultation with an asthma specialist (e.g., allergist, immunologist, pulmonologist) or rheumatologist

AND

4. Documentation of one of the following:
    a. Sustained severe disease (e.g., vasculitis with cerebral, cardiac, renal, or gastrointestinal involvement)
    b. Disease flares with tapering of corticosteroid therapy or immunotherapy

Hypereosinophilic Syndrome

1. Documented diagnosis of hypereosinophilic syndrome

AND

2. Documentation that non-hematologic secondary causes have been ruled out

AND

3. Member is at least 12 years of age

AND

4. Documentation of one of the following:
    a. Pre-treatment blood eosinophil count of at least 1,500 cells/mcL on two different examinations separated by one month
    b. Pathologic diagnosis on tissue exam

AND

5. Documented trial and failure of, contraindication to, or clinical inappropriateness with treatment with at least one of the following: oral corticosteroids, immunosuppressive therapy, or cytotoxic therapy

APPENDIX

NHBLI Estimated Comparative Daily Dosages for Inhaled Corticosteroids in Adults

Drug	High Daily Dose (Adult ≥ 12 years old)
Beclomethasone HFA 40 or 80 mcg/puff	>320 mcg
Budesonide DPI 90 or 180 mcg/inhalation	>720 mcg
Ciclesonide HFA 80 or 160 mcg/puff	>320 mcg
Flunisolide HFA 80 mcg/puff	>640 mcg
Fluticasone propionate HFA 44, 110, 220 mcg/puff	>440 mcg
Fluticasone propionate DPI 50, 100, 250 mcg/inhalation 55, 113, 232 mcg/inhalation	>500 mcg
Fluticasone furoate DPI 50, 100, 200 mcg/inhalation	200 mcg
Mometasone DPI 110, 220 mcg/actuation	>440 mcg
Mometasone HFA 100, 200 mcg/actuation	>400 mcg

DPI: dry powder inhaler, HFA: hydrofluoroalkane

LIMITATIONS

- Coverage will not be authorized if the Member is also receiving another biologic mediation for the treatment of asthma (e.g., Dupixent, Xolair). Combination respiratory interleukin therapy will not be authorized.
- Documentation of a Member being a social drinker does not qualify as a medically acceptable contraindication or clinical inappropriateness to methotrexate therapy.
- For the treatment of severe asthma and eosinophilic granulomatosis with polyangiitis, initial coverage of a respiratory interleukin will be authorized for 6 months. Reauthorization of a respiratory interleukin will be provided in 12-month intervals.
- Members new to the plan stable on a respiratory interleukin should be reviewed against Reauthorization Criteria for all indications.

CODES

The following HCPCS/CPT code(s) are:

Code	Description
J2182	Injection, mepolizumab, 1 mg
J2786	Injection, reslizumab, 1 mg
J0517	Injection, benralizumab, 1 mg

Note: Medical billing codes may not be used for Fasenra autoinjector and Nucala pre-filled autoinjectors and glass syringes for self-administration. These formulations must be obtained via the Member's pharmacy benefit.

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APPROVAL HISTORY

September 13, 2016: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. January 1, 2017: Administrative update: added new J code (J2786) to Medical Necessity Guideline and removed expired C code (C9481).
2. April 11, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether.
3. August 8, 2017: No changes.
4. August 7, 2018: Effective January 1, 2019, created therapeutic class Medical Necessity Guideline and changed name of Medical Necessity Guideline to "Respiratory Interleukins: Cinqair® (reslizumab), Fasenra™ (benralizumab), Nucala® (mepolizumab)". Coverage criteria to be applied consistently to all respiratory interleukins were created. Additional drug specific criteria changes include specifying that the pre-treatment serum eosinophil count for Cinqair must be within the past 6 weeks. Removed documentation of a spectrum eosinophilic count greater than 3% from Nucala's additional drug specific criteria. Administrative updates to Limitations section to make wording appropriate for a therapeutic Medical Necessity Guideline.
5. November 13, 2018: Effective January 1, 2019, updated specialist requirements to allow for the prescription to be written by or in consultation with an asthma specialist. Removed annual reauthorization criteria that require documentation that the patient has been seen within the previous 14 months and there is continued documented benefit from using the requested agent. Removed the following Note from the criteria: "An adherent trial is defined as a medication possession ratio (MPR) ≥70% based on the previous 120 days of prescription claims (records will be required for approval)." Removed the following Limitation from the criteria: "Other causes of eosinophilia such as hypereosinophilic syndromes, neoplastic disease, or parasitic disease must be ruled out." Updated the Appendix table based on updated clinical information.
6. January 1, 2019: Administrative update: added new J code J0517 to Medical Necessity Guideline and removed expired C code C9466 from the Medical Necessity Guideline.
7. April 9, 2019: For Cinqair and Fasenra for maintenance treatment of severe asthma, removed the requirement that pre-treatment serum eosinophil count is measured within 6 weeks prior to initiation of treatment. For Nucala for maintenance treatment of severe asthma, updated the criteria to require a pre-treatment serum eosinophil count of ≥150 cells/mcL.
8. August 13, 2019: Added the following Note to the Codes section "Medical billing codes may not be used for Nucala pre-filled autoinjectors and glass syringes for self-administration. These formulations must be obtained via the Member's pharmacy benefit."
9. October 15, 2019: Updated coverage criteria for Nucala to require Member is at least 6 years of age based on updated package labeling.
10. April 14, 2020: Effective July 1, 2020, modified reauthorization criteria for all indications and added the following Limitation "Members new to the plan stable on a respiratory interleukin should be reviewed against Reauthorization Criteria for all indications." Consolidated the coverage criteria for asthma to eliminate separate requirements for documentation of poor asthma control or recurrent exacerbations and prerequisite therapies and removed requirement for documentation the Member is receiving other treatments for asthma. Removed the following Limitation: "Cinqair (reslizumab) will only be covered when administered in a healthcare setting by a healthcare professional equipped to manage anaphylaxis." Updated the Limitation to: "Coverage will not be authorized if the Member is also receiving another biologic mediation for the treatment of asthma (e.g., Dupixent, Xolair). Combination respiratory interleukin therapy will not be authorized."
11. November 10, 2020: Added coverage criteria for Nucala's supplemental indication for the treatment of hypereosinophilic syndrome.
12. December 8, 2020: Effective January 1, 2021, Tufts Health Together removed from the Medical Necessity Guideline.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based

on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

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