POLICY: Immunologicals – Cinqair® (reslizumab injection for intravenous use – Teva Respiratory)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 05/08/2025

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW
Cinqair, an interleukin-5 antagonist monoclonal antibody, is indicated for **severe asthma** as add-on maintenance treatment of patients ≥ 18 years of age who have an eosinophilic phenotype.[1] Limitations of Use: Cinqair is not indicated for the treatment of other eosinophilic conditions or for the relief of acute bronchospasm/status asthmaticus.

Clinical Efficacy

The Cinqair pivotal studies included adult and adolescent patients with moderate to severe asthma who had baseline blood eosinophil levels ≥ 400 cells/microliter despite therapy.[2-4] In one study that did not require patients to have elevated eosinophils at baseline, clinical benefit in regard to forced expiratory volume in 1 second (FEV_1) was not statistically significant with Cinqair vs. placebo. However, a significant improvement was observed in a subgroup of patients with baseline eosinophil levels ≥ 400 cells/microliter.

Guidelines

The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2024) proposes a step-wise approach to asthma treatment.[5] Cinqair is listed as an option for add-on therapy in patients ≥ 18 years of age with severe eosinophilic asthma. Severe asthma is defined as asthma that is uncontrolled despite adherence to optimized high-dose inhaled corticosteroid (ICS)/long-acting $beta_2$-agonist (LABA) therapy or that worsens when high-dose treatment is decreased. Higher blood eosinophil levels, higher number of severe exacerbations in the previous year, adult-onset asthma, nasal polyps, maintenance oral corticosteroid requirements, and low lung function may predict a good asthma response to Cinqair.

According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), severe asthma is defined as asthma which requires treatment with a high-dose ICS in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy.[6,7] Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20;
2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;

3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
4) Airflow limitation: FEV_1 < 80% predicted after appropriate bronchodilator withholding.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Cinqair. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the durations noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Cinqair, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Cinqair to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Cinqair is recommended for requests meeting both the preferred product step therapy requirements and indication requirements

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Preferred Product(s): Fasenra and Nucala
Non-Preferred Products(s): Cinqair

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient meets any *one of the items listed below (A, B, C, D or E)*. *Chart notes documenting* the issue must be provided at time of request:

A. The patient is *not* considered a new start to the non-preferred product (new start is defined as no use of the requested product in the previous 365 days) OR

B. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

D. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

E. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products.
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indication

1. Asthma. Approve Cinqair for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):

i. Patient is ≥ 18 years of age; AND

ii. Patient meets ONE of the following (a or b):

a) Patient has a blood eosinophil level ≥ 400 cells per microliter within the previous 4 weeks; OR

b) Patient had a blood eosinophil level ≥ 400 cells per microliter prior to treatment with Cinqair or another monoclonal antibody therapy that may alter blood eosinophil levels; AND

Note: Examples of monoclonal antibody therapies that may alter blood eosinophil levels include Cinqair, Adbry (tralokinumab-ldrm subcutaneous injection), Dupixent (dupilumab subcutaneous injection), Ebglyss (lebrikizumab-lbkz subcutaneous injection), Fasenra (benralizumab subcutaneous injection), Nemluvio (nemolizumab-ilto subcutaneous injection), Nucala (mepolizumab subcutaneous injection), Tezspire (tezepelumab-ekko subcutaneous injection), and Xolair (omalizumab subcutaneous injection).

iii. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):

a) An inhaled corticosteroid; AND

b) At least one additional asthma controller or asthma maintenance medication; AND

Note: Examples of additional asthma controller or asthma maintenance medications are inhaled long-acting $beta_2$-agonists, inhaled long-acting muscarinic antagonists, and monoclonal antibody therapies (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire, Xolair). Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill the requirement for both criteria a and b.

iv. Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d, or e):

Note: "Baseline" is defined as prior to receiving Cinqair or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Cinqair, Dupixent, Fasenra, Nucala, Tezspire, and Xolair.

a) Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR

b) Patient experienced one or more asthma exacerbation(s) requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous year; OR

c) Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR

d) Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR

e) Patient has asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND

v. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; OR

B) Patient is Currently Receiving Cinqair. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has already received at least 6 months of therapy with Cinqair; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Cinqair should be considered under criterion 1A (Asthma, Initial Therapy).

ii. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination; AND

iii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a response to Cinqair therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department, urgent care, or medical clinic visits due to asthma; and decreased requirement for oral corticosteroid therapy.

Dosing. Approve 3 mg/kg administered intravenously once every 4 weeks.

Conditions Not Recommended for Approval

Coverage of Cinqair is not recommended in the following situations:

1. **Concurrent use of Cinqair with another Monoclonal Antibody Therapy.** The efficacy and safety of Cinqair used in combination with other monoclonal antibody therapies have not been established.
   Note: Monoclonal antibody therapies are Adbry® (tralokinumab-ldrm subcutaneous injection), Dupixent® (dupilumab subcutaneous injection), Ebglyss® (lebrikizumab-lbkz subcutaneous injection), Fasenra® (benralizumab subcutaneous injection), Nemluvio® (nemolizumab-ilto subcutaneous injection), Nucala® (mepolizumab subcutaneous injection), Tezspire® (tezepelumab-ekko subcutaneous injection), or Xolair® (omalizumab subcutaneous injection).

2. **Eosinophilic Esophagitis or Eosinophilic Gastroenteritis.** Cinqair is not indicated for the treatment of eosinophilic conditions other than asthma.[1] In addition to data from a small pilot study and from a small compassionate use program, one randomized, double-blind, placebo-controlled study (n =226) evaluated the efficacy of Cinqair in pediatric and adolescent patients with eosinophilic esophagitis.[8-10] In this study, patients were randomly assigned to receive Cinqair IV at varying doses for 12 weeks. At Week 15, peak esophageal eosinophil counts were reduced from

baseline and all reductions with Cinqair were significant compared with placebo. Improvements in physician's global assessment scores were also observed in all groups (including placebo), but the difference between Cinqair and placebo was not statistically significant. Clinical guidelines on the diagnosis and management of eosinophilic esophagitis from the American College of Gastroenterology (2025) do not make a recommendation for or against Cinqair citing inconsistent data.[11] Additional, well-controlled trials are needed to determine the role of Cinqair in the treatment of eosinophilic esophagitis and eosinophilic gastroenteritis.

3. **Hypereosinophilic Syndrome.** Cinqair is not indicated for the treatment of eosinophilic conditions other than asthma.[1] One very small pilot study (n = 4) evaluated the safety and efficacy of Cinqair in patients with hypereosinophilic syndrome who were refractory to or intolerant of treatment with conventional therapy.[12] A single dose of Cinqair resulted in a response in two of four patients. In the two responders, blood eosinophil counts dropped to within the normal range within 48 hours of the Cinqair infusion and this was accompanied by an improvement in clinical signs and symptoms. The World Health Organization (WHO) and international consensus classification of eosinophilic disorders update on diagnosis, risk stratification, and management (2024) notes that Cinqair has not been evaluated extensively for the treatment of hypereosinophilic syndrome.[13] At this time, the WHO considers Cinqair investigational for the treatment of hypereosinophilic syndrome. Additional, well-controlled trials are needed to determine the role of Cinqair in the treatment of hypereosinophilic syndrome.

4. **Nasal Polyps.** Cinqair is not indicated for the treatment of nasal polyps.[1] One double-blind, placebo-controlled, randomized safety and pharmacokinetic study (n = 24) evaluated the use of Cinqair in patients with nasal polyps.[14] Patients received a single infusion of either Cinqair 3 mg/kg, Cinqair 1 mg/kg, or placebo. It was reported that blood eosinophil counts and concentrations of eosinophil cation protein were reduced for up to 8 weeks following the Cinqair infusion. Nasal polyp scores improved for approximately 4 weeks in one-half of patients receiving active treatment. Additionally, a pooled subgroup analysis from the two pivotal Cinqair asthma exacerbation trials found that in patients with inadequately controlled asthma and chronic sinusitis with nasal polyps (n = 150) Cinqair demonstrated enhanced efficacy. Patients in this subgroup experienced an 83% reduction in the clinical asthma exacerbation rate with Cinqair vs. placebo.[15] The magnitude of this reduction was greater than that observed with the overall study population. The Joint Task Force on Practice Parameters published guidelines for the medical management of chronic rhinosinusitis with nasal polyps in 2023.[16] Use of other anti-interleukin-5 antagonist monoclonal antibodies is recommended. However, no recommendations are provided for Cinqair.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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16. Rank MA, Chu DK, Bognanni A, et al. Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. *J Allergy Clin Immunol*. 2023;151(2):386-398.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	• Updated initial therapy criteria for "Asthma in Patients with Severe Disease and an Eosinophilic Phenotype" to more concisely state the previous therapies required. Added the following: NOTE: An exception to the requirement for a trial of one additional asthma controller/maintenance medication (criterion b) can be made if the patient has already received anti-IL-5 therapy (e.g., Cinqair, Fasenra, Nucala) used concomitantly with an ICS for at least 3 consecutive months. • Updated dosing for "Asthma in Patients with Severe Disease and an Eosinophilic Phenotype". Removed the requirement that the Cinqair be infused over 20 to 50 minutes.	02/20/2019
Selected Revision	• **Asthma**: Approval indication was changed from "Asthma in Patients with Severe Disease and an Eosinophilic Phenotype" to "Asthma". Wording in reference to "according to the prescribing physician" was changed to "according to the prescriber". Added Wixela Inhub, a generic to Advair Diskus, to list of examples of asthma controller/maintenance medications.	10/23/2019
Early Annual Revision	• **Asthma**: Removed lists of examples of inhaled asthma controller/maintenance medications. • **Hypereosinophilic Syndrome**: Condition Not Recommended for Approval was changed from "Hypereosinophilic Syndrome, Idiopathic" to "Hypereosinophilic Syndrome".	02/12/2020
Annual Revision	No criteria changes.	2/17/2021
Annual Revision	No criteria changes.	03/16/2022
Selected Revision	**Asthma:** Criteria for a blood eosinophil level ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to any anti-interleukin-5 therapy was changed to prior to any treatment with Cinqair or another	07/20/2022

	monoclonal antibody therapy that may lower blood eosinophil levels. Throughout criteria, updated notes to include examples of monoclonal antibody therapies to include Dupixent (dupilumab subcutaneous injection), Tezspire (tezepelumab-ekko subcutaneous injection), Adbry (tralokinumab-ldrm subcutaneous injection), and Xolair® (omalizumab subcutaneous injection). Criteria requiring the patient to have experienced one or more asthma exacerbation(s) requiring a hospitalization or an emergency department visit in the previous year, were updated to include an urgent care visit as well. **Conditions Not Recommended for Approval:** Criteria were updated to recommend against use of Cinqair with another monoclonal antibody therapy. Previously, criteria listed anti-interleukin monoclonal antibody therapies and Xolair separately.	
Annual Revision	**Conditions not recommended for approval:** Criteria were updated to clarify that use of Cinqair with another monoclonal antibody therapy is specific to Fasenra, Nucala, Dupixent, Tezspire, Xolair, and Adbry.	03/22/2023
Annual Revision	**Asthma:** Removed leukotriene receptor antagonists as an example of additional asthma controller or asthma maintenance medications.	04/19/2024
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024
Annual Revision	**Asthma:** Eosinophil level requirements were clarified to require a level ≥ 400 cells/microliter either within the previous 6 weeks OR prior to treatment with a monoclonal antibody that may alter eosinophil levels. Previously, criteria required a level ≥ 150 cells/microliter either within the previous 6 weeks OR within 6 weeks prior to treatment with a monoclonal antibody that may lower eosinophil levels. Throughout the policy, Ebglyss (lebrikizumab-lbkz subcutaneous injection) and Nemluvio (nemolizumab-ilto subcutaneous injection) were added to notes as examples of monoclonal antibody therapies.	04/09/2025
Aspirus Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/08/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025

IL – Interleukin; ICS – Inhaled corticosteroid.