Drug Coverage Policy

Effective Date.....7/15/2025
Coverage Policy Number.....IP0423
Policy Title.....Cinqair

Immunologicals – Cinqair

- Cinqair® (reslizumab intravenous infusion - Teva Respiratory)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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 (2023) 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 (i.e., patients who continue to experience exacerbations or have poor symptom control despite treatment with a high-dose ICS/long-acting $beta_2$-agonist [LABA] and who have eosinophilic biomarkers or require therapy with maintenance oral corticosteroids). Higher blood eosinophil levels, higher number of severe exacerbations in the previous year, adult-onset asthma, nasal polyposis, 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: FEV1 < 80% predicted after appropriate bronchodilator withholding.

Coverage Policy

Policy Statement
Prior Authorization is recommended for prescription benefit coverage of Cinqair. All approvals are provided for the duration 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, approval requires Cinqair to be prescribed by a physician who has consulted with or who specializes in the condition.

Cinqair is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Asthma.** Approve Cinqair for the duration noted if the patient meets one of the following conditions (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, vi and vii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has a history of ONE of the following (a or b):
       - **a)** Patient meets BOTH of the following (1 and 2):
         - **(1)** Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; AND
           Note: The reduced FEV_1 should not be due to smoking-related chronic obstructive pulmonary disease.
         - **(2)** Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR
       - **b)** Patient meets ONE of the following (1, 2, 3, 4, or 5)
         - **(1)** Increase of > 12% and > 200ml in FEV_1 following administration of a standard dose of a short-acting bronchodilator; OR
         - **(2)** Increase of > 12% and > 200ml in FEV_1 between prescriber visits; OR
         - **(3)** Increase of > 12% and > 200ml in FEV_1 from baseline to after at least 4 weeks of asthma treatment; OR
         - **(4)** Positive exercise challenge testing; OR
         - **(5)** Positive bronchial challenge testing; AND

       Note: The above lung function criteria may be met at any time prior to or during asthma treatment.
     - **iii.** Patient has a blood eosinophil count ≥ 400 cells per microliter within the previous 4 weeks or prior to treatment with Cinqair or another monoclonal antibody therapy that may lower blood eosinophil levels; AND
       Note: Examples of monoclonal antibody therapies that may lower 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).
     - **iv.** Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
       a) An inhaled medium- or high- dose 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 a medium- or high- dose inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill the requirement for both criteria a and b.
     - **v.** Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, or c):
       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 asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND

vi. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist.

vii. Preferred product criteria are met for the product(s) as listed in the below table(s)

B) Patient is Currently Receiving Cinqair. Approve for 1 year if the patient meets 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.

Employer Plans:

Product	Criteria
Cinqair (reslizumab for intravenous injection)	**1. ONE** of the following (A or B): **A.** Patient has tried **ONE** of the following (i or ii): **i.** Nucala [may require prior authorization] **ii.** Fasenra [may require prior authorization] **B.** Patient has already been started on therapy with Cinqair

Individual and Family Plans:

Product	Criteria
Cinqair (reslizumab for intravenous injection)	**1. ONE** of the following (A or B): **A.** Patient has tried **ONE** of the following (i or ii): **i.** Nucala [may require prior authorization] **ii.** Fasenra [may require prior authorization] **B.** Patient has already been started on therapy with Cinqair

Conditions Not Covered

Cinqair for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as newly published data are available.

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), Fasenra® (benralizumab 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. Guidelines for the management of eosinophilic esophagitis from the American Gastroenterological Association and the Joint Task Force on Allergy Immunology Practice Parameters (2020) only recommend using anti-interleukin-5 therapies in the context of a clinical trial.[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 CRSwNP in 2023.[16] Use of other anti-interleukin-5 antagonist monoclonal antibodies is recommended. However, no recommendations are provided for Cinqair.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2786	Injection, reslizumab, 1 mg

References

1. Cinqair® injection for intravenous use [prescribing information]. Frazer, PA: Teva Respiratory; January 2019.
2. Castro M, Zangrilli J, Wechsler ME, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicenter, parallel, double-blind, randomized, placebo-controlled, phase 3 trials. *Lancet Respir Med*. 2015; 3:355-366.
3. Bjermer L, Lemiere C, Maspero J, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil levels: a randomized phase 3 study. *Chest*. 2016;150(4):789-798.
4. Corren J, Weinstein S, Janka L, et al. Phase 3 study of reslizumab in patients with poorly controlled asthma: effects across a broad range of eosinophil counts. *Chest*. 2016;150(4):799-810.
5. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2023. Available at: http://www.ginasthma.org. Accessed on April 8, 2024.
6. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014; 43:343-373.
7. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society Guideline. *Eur Respir J.* 2020; 55:1900588.
8. Prussin C, James SP, Huber MM, et al. Pilot study of anti-IL-5 in eosinophilic gastroenteritis. *J Allergy Clin Immunol*. 2003;111: S275.
9. Spergel JM, Rothenberg ME, Collins MH, et al. Reslizumab in children and adolescents with eosinophilic esophagitis: results of a double-blind, randomized, placebo-controlled trial. *J Allergy Clin Immunol*. 2012;129(2):456-463.
10. Markowitz JE, Jobe L, Miller M, et al. Safety and efficacy of reslizumab for children and adolescents with eosinophilic esophagitis treated for 9 years. *J Pediatr Gastroenterol Nutr*. 2018;66(6):893-897.
11. Hirano I, Chan ES, Rank MA, et al. AGA Institute and Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158(6):1776-1786.
12. Klion AD, Law MA, Noel P, et al. Safety and efficacy of the monoclonal anti-interleukin-5 antibody SCH55700 in the treatment of patients with hypereosinophilic syndrome. *Blood*. 2004;103(8):2939-2941.
13. Shomali W, Gotlib J. World Health Organization and international consensus classification of eosinophilic disorders: 2024 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2024;99(5):946-968.
14. Gevaert P, Lang-Loidolt D, Lackner A, et al. Nasal IL-5 levels determine the response to anti-IL-5 treatment in patients with nasal polyps. *J Allergy Clin Immunol*. 2006;118(5):1133-1141.
15. Weinstein SF, Katial RK, Bardin P, et al. Effects of reslizumab on asthma outcomes in a subgroup of eosinophilic asthma patients with self-reported chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol Pract*. 2019;7(2):589-596.
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.

Revision Details

Type of Revision	Summary of Changes	Date

Annual Revision	**Updated** coverage policy title from *Reslizumab* to *Immunologicals – Cinqair.* **<u>Asthma:</u>** **Updated** diagnostic criteria requirements for confirmation of asthma. **Updated** initial approval authorization duration from 12 months to 6 months. **<u>Conditions Not Covered:</u>** **Removed** *Atopic Dermatitis* from *Conditions Not Covered*.	9/1/2024
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 ≥ 400 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. **Added** Ebglyss and Nemluvio as options/ examples of monoclonal antibody therapies that may alter blood eosinophil levels to "Notes" throughout policy.	7/15/2025

The policy effective date is in force until updated or retired.