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

**EFFECTIVE DATE:** 1/1/2020
**LAST REVISION DATE:** 09/16/2024

**COVERAGE CRITERIA FOR:** All UCare 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 (2022) 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 difficult-to-treat, severe eosinophilic asthma (i.e., asthma that cannot be managed by therapy with medium- to high-dose inhaled corticosteroid [ICS]/formoterol [as both maintenance and reliever therapy] or medium- to high-dose ICS/long-acting $beta_2$-agonist [LABA] combination therapy with an as needed short-acting $beta_2$-agonist reliever, with or without an additional controller). Higher blood eosinophil levels, more exacerbations in the previous year, adult-onset asthma, nasal polyposis, a maintenance corticosteroid requirement at baseline, and low lung function (i.e., $FEV_1$ < 65% of predicted) 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.

**RECOMMENDED AUTHORIZATION CRITERIA**

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

---

**Step Therapy Requirements (New Starts Only)**

**Criteria.** *The patient must meet the following criteria (A or B):*

**A.** For patients new to Cinqair therapy only, must have a trial of Fasenra or Nucala prior to approval of Cinqair. New starts to therapy defined as no use of Cinqair within the past 180 days for Medicaid and Commercial patients and no use of Cinqair within the past 365 days for Medicare patients.

**B.** Patient has a contraindication or other clinical reason why Fasenra or Nucala cannot be tried before Cinqair.

Note: Step only required for indications FDA-Approved for both Cinqair and the preferred product(s).

**FDA-Approved Indications**

---

**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, and v):

**i.** Patient is ≥ 18 years of age; AND

**ii.** Patient has a blood eosinophil count ≥ 400 cells per microliter within the previous 4 weeks or within 4 weeks 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), Fasenra (benralizumab 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.

**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.

---

**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), Fasenra® (benralizumab subcutaneous injection), Nucala® (mepolizumab subcutaneous injection), Teszpire® (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 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.

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

## 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.

**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.<br>• 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.<br>• **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 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.<br>**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. | 07/20/2022 |
| 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 |
| UCare P&T Review | Policy reviewed and approved by UCare P&T committee. Annual review process | 09/16/2024 |

IL – Interleukin; ICS – Inhaled corticosteroid.