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Reslizumab

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated, and coverage is not required for non-formulary drugs.

Coverage

Intravenous infusion of reslizumab (Cinqair®) **may be considered medically necessary** for the add-on maintenance treatment of patients with severe eosinophilic asthma when **ALL** the following criteria are met:

- Individual is 18 years of age or older; AND
- There is documented and current use of an inhaled corticosteroid (ICS) in combination with a long acting beta2-agonist (LABA), leukotriene receptor antagonist [LTRA], theophylline or long-acting muscarinic antagonist (LAMA); AND
- The individual has uncontrolled asthma while on control therapy as evidenced by two or more exacerbations requiring systemic glucocorticoids, frequent ER visits, or hospitalizations (see **NOTE 1**); AND
- Eosinophil count of ≥ 400 cells/µL (within 3 to 4 weeks of dosing).

NOTE 1: Individuals who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also meet this definition of moderate to severe asthma. For definition of uncontrolled asthma see Description section.

Reslizumab (Cinqair®) **is considered experimental, investigational and/or unproven** for all other non-FDA approved indications.

Policy Guidelines

None.

Description

There are multiple monoclonal antibodies (mAbs) that are currently available for use as add-on treatment for severe asthma. These mAbs either bind or block the offending triggers to reduce allergic cascade and airway inflammation when eosinophils are the causative factor.

Background

According to the Asthma and Allergy Foundation of America, asthma affects nearly 28 million people in the United States with roughly 82.14% of adults and 17.5% of children affected. Asthma has been increasing since the early 1980s in all age, sex and racial groups. It is a chronic disease that causes the airways to become inflamed, making it hard to breathe. There is no cure

for asthma. The best way to manage asthma is to avoid triggers, take medications to prevent symptoms, and prepare to treat asthma episodes if they occur. (2)

Asthma symptoms can appear when the individual is exposed to a trigger. A trigger is something that the individual is sensitive to, which causes swelling, mucous production and narrowing within the airways. Common asthma triggers are pollen, chemicals, extreme weather changes, smoke, dust mites, stress and exercise.

Definition of Uncontrolled Asthma

At least one of the following:

- Poor symptom control: Asthma Control Questionnaire (ACQ) score consistently >1.5, Asthma Control Test (ACT) score <20 (or ''not well controlled'' by the National Asthma Education and Prevention Program (NAEPP) /Global Initiative for Asthma (GINA) guidelines);
- Frequent severe exacerbations: ≥2 bursts of systemic corticosteroids (CS) (>3 days each) in the previous year;
- Serious exacerbations: at least 1 hospitalization, intensive care unit (ICU) stay, or mechanical ventilation in the previous year;
- Airflow limitation: after appropriate bronchodilator withhold, forced expiratory volume in 1 second (FEV_1) <80% predicted (in the face of reduced FEV_1/forced vital capacity (FVC) defined as less than the lower limit of normal). (3)

Regulatory Status

Reslizumab (Cinqair®) (Teva Pharmaceuticals, Frazer, PA) was approved by the U.S. Food and Drug Administration on March 23, 2016. Cinqair® is an interleukin 5 antagonist monoclonal antibody (IgG4 kappa) indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. Limitations of use include treatment of other eosinophilic conditions or relief of acute bronchospasm or status asthmaticus. (1)

Cinqair is administered via intravenous infusion every four weeks in a clinical setting prepared to manage anaphylactic reactions.

Rationale

This medical policy was created in 2016 and is based off the U.S. Food and Drug Administration labeled indications for reslizumab (Cinqair).

Cinqair® (1)

The asthma development program for Cinqair 3 mg/kg (administered once every 4 weeks) included 4 randomized, double-blind, placebo-controlled studies (Studies I-IV) 16 to 52 weeks in duration involving 981 patients 12 years of age and older. While patients aged 12 to 17 years were included in these trials, Cinqair is not approved for use in this age group. All subjects continued their background asthma therapy throughout the duration of the studies.

Studies I and II

Studies I and II were 52-week studies in 953 patients with asthma who were required to have a blood eosinophil count of at least 400 cells/µl (within 3 to 4 weeks of dosing), and at least 1 asthma exacerbation requiring systemic corticosteroid use over the past 12 months. The majority of patients (82%) were on medium to high dose of inhaled corticosteroids (ICS) plus a long-acting beta agonist (ICS/LABA) at baseline. Maintenance oral corticosteroids (OCS) (up to 10 mg of prednisone per day or equivalent) were allowed; 106 (11%) patients were on OCS at baseline. Cinqair 3 mg/kg administered once every 4 weeks for a total of 13 doses was evaluated compared with placebo.

Study III

Study III was a 16-week study in 315 patients who were required to have a blood eosinophil count of at least 400/mcL at screening (within 3 to 4 weeks of dosing). Maintenance OCS were not allowed. Cinqair 3 mg/kg or 0.3 mg/kg administered once every 4 weeks for a total of 4 doses was evaluated compared with placebo. While 2 doses of Cinqair were studied, Cinqair 3 mg/kg is the only recommended dose.

Study IV

Study IV was a 16-week study in 496 patients unselected for baseline blood eosinophil levels (approximately 80% of patients had a screening [within 3 to 4 weeks of dosing] blood eosinophil count of less than 400/mcL). Maintenance OCS were not allowed. Cinqair 3 mg/kg administered once every 4 weeks for a total of 4 doses was evaluated compared with placebo.

The demographics and baseline characteristics of these 4 studies is provided in Table 1.

Table 1. Demographics and Baseline Characteristics of Patients in Asthma Studies

	Study I (N=489)	**Study II (N=464)**	**Study III (N=315)**	**Study IV (N=496)**
Mean age (year)	47	47	44	45
Female (%)	63	63	58	64
White (%)	73	73	81	67
Duration of asthma, mean (year)	19	18	20	26
Baseline Pre-bronchodilator FEV_1, mean % predicted[a]	64	69	70	67
Baseline Reversibility, mean % Δ FEV_1 post-SABA[a]	26	28	25	26
Baseline mean blood eosinophil count/mcL[a]	660	649	614	280
Mean number of exacerbations in previous year	1.99	1.94	2.03	1.86

FEV_1: forced expiratory volume in 1 second; SABA: short-acting beta agonist.

[a] Baseline for lung function and eosinophil count is the day of randomization.

All patients had to be on inhaled corticosteroid (ICS) background therapy and could have been receiving any combination of background therapies (ICS with or without another controller [non-ICS and/or OCS]).

Exacerbations

The primary endpoint for Studies I and II was the frequency of asthma exacerbations for each patient during the 52-week treatment period. An asthma exacerbation was defined as a worsening of asthma that required at least 1 of the following medical interventions: 1) Either the use of a systemic corticosteroid, or ≥ 2-fold an increase in the use of ICS for 3 or more days, and/or 2) Asthma-related emergency treatment including at least 1 of the following: an unscheduled visit to their healthcare professional for nebulizer treatment or other urgent treatment to prevent worsening of asthma symptoms; a visit to the emergency room for asthma-related treatment; or an asthma-related hospitalization. The medical intervention had to be corroborated with at least 1 of the following: 1) a decrease in forced expiratory volume in 1 second (FEV1) by 20% or more from baseline, 2) a decrease in peak expiratory flow rate (PEFR) by 30% or more from baseline on 2 consecutive days, or 3) worsening of symptoms or other clinical signs per physician evaluation of the event.

In Studies I and II, patients receiving Cinqair 3 mg/kg administered once every 4 weeks had significant reductions in the rate of all asthma exacerbations compared to placebo (Table 2). Exacerbations requiring the use of a systemic corticosteroid (e.g., OCS) as well as exacerbations resulting in hospitalization or an emergency room visit were each reduced with Cinqair 3 mg/kg.

Table 2. Frequency of Asthma Exacerbations during the 52-Week Treatment Period in Patients with Severe Asthma with an Eosinophilic Phenotype (Studies I and II)[a]

	Treatment Arm	Asthma Exacerbation Rate	Rate Ratio (95% CI)
All exacerbations			
Study I	Cinqair 3 mg/kg (n=245)	0.90	0.5 (0.37, 0.67)
	Placebo (n=244)	1.80	
Study II	Cinqair 3 mg/kg (n=232)	0.86	0.41 (0.28, 0.59)
	Placebo (n=232)	2.11	
Exacerbations requiring systemic corticosteroid use			
Study I	Cinqair 3 mg/kg (n=245)	0.72	0.45 (0.33, 0.62)
	Placebo (n=244)	1.60	
Study II	Cinqair 3 mg/kg (n=232)	0.65	0.39 (0.27, 0.58)
	Placebo (n=232)	1.66	
Exacerbations resulting in a hospitalization AND/OR emergency room visit			
Study I	Cinqair 3 mg/kg (n=245)	0.14	0.66 (0.32, 1.36)
	Placebo (n=244)	0.21	
Study II	Cinqair 3 mg/kg (n=232)	0.03	0.69 (0.29, 1.65)
	Placebo (n=232)	0.05	

CI: Confidence interval.
[a] Randomized patients

The proportion of patients who did not experience an asthma exacerbation during the 52-week treatment period was higher in the Cinqair 3 mg/kg group (62% and 75%) compared with the placebo group (46% and 55%), in Studies I and II, respectively. The time to first asthma exacerbation was significantly longer for the groups receiving Cinqair 3 mg/kg compared with placebo in both Studies I and II.

Lung Function
The effect of Cinqair 3 mg/kg administered once every 4 weeks on FEV1 over time relative to placebo was assessed in all 4 studies. FEV1 was the primary endpoint in the 16-week lung function studies: Study III and Study IV.

Study III also studied a lower dose, Cinqair 0.3 mg/kg, that produced significant but numerically smaller changes in FEV1, and blood eosinophil reduction compared with the 3 mg/kg dose. While 2 doses of Cinqair were studied, Cinqair 3 mg/kg is the only recommended dose.

Study IV was the only study to test Cinqair 3 mg/kg in asthma patients unselected for blood eosinophils (measured 3 to 4 weeks prior to dosing); association of treatment effect (i.e., difference between Cinqair and placebo in the change in FEV1 at Week 16) and baseline blood eosinophils was not observed.

Improvements in FEV1 were observed at 4 weeks following the first dose of CINQAIR for Studies I and II and maintained through Week 52.

The Asthma Control Questionnaire-7 (ACQ-7) and Asthma Quality of Life Questionnaire (AQLQ) were both assessed in Studies I, II, and III. The responder rate for both measures was defined as an improvement in score of 0.5 or more as threshold over 16 weeks.
• For ACQ-7, the responder rate for those randomized to Cinqair vs. placebo was 69% vs. 65% for Study I, 70% vs. 58% for Study II, and 64% vs. 58% for Study III.
• For AQLQ, the responder rate for those randomized to Cinqair vs. placebo was 66% vs. 58% for Study I, 67% vs. 55% for Study II, and 64% vs. 48% for Study III.

Summary of Evidence
Based on the U.S. FDA labeled indications, reslizumab (Cinqair®) is indicated for add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. Reslizumab (Cinqair®) is considered experimental, investigational and/or unproven for all other non-FDA approved labeled indications.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J2786

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. FDA – Highlights of prescribing information. Reslizumab (Cinqair) (January 2019). Available at <https://www.accessdata.fda.gov> (accessed July 21, 2025).

Other:

2. Asthma and Allergy Foundation of America. Asthma. (Updated March 2023). Available at <https://www.aafa.org> (accessed July 21, 2025).
3. Narasimhan K. Difficult-to-Treat and Severe Asthma: Management Strategies. Am Fam Physician. 2021; 103(5):286-290. Available at <https://www.aafa.org> (accessed July 24, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
11/15/2025	Document updated with literature review. The following change was made to Coverage: Removed statement for continuation therapy; revised coverage criteria for medically necessary statement; revised EIU statement; and removed note 2. Reference 3 added; others removed.

05/01/2025	Document updated. The following changes were made to Coverage: 1) Added criteria for continuation therapy; and 2) Added the following under Initial Therapy: "Individual has tried and failed, or has a clinical reason to avoid subcutaneous injection of benralizumab (Fasenra®) or mepolizumab (Nucala®); AND"; and added "dupilumab [Dupixent]" and "tezepelumab-ekko [Tezspire]" to list of monoclonal antibody agent examples that reslizumab should not be used in combination with. No new references added.
05/01/2024	The following change was made to Coverage: Modified medically necessary coverage criteria. No new references added; some updated.
07/01/2023	Document updated with literature review. Coverage unchanged. Reference 7 updated; one reference removed.
01/15/2023	Reviewed. No changes.
08/01/2021	Document updated with literature review. The following change was made to Coverage: Removed continuation criteria. No new references added; some updated.
11/15/2020	Document updated with literature review. The following changes were made to Coverage: 1) Modified medically necessary conditional criteria; and 2) Modified NOTE 1 to read: "Patients who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also meet this definition of severe asthma. For definition of uncontrolled asthma see Description section." The following references were added/updated: 1-2, 4, and 8. Title changed from "Reslizumab (Cinqair)".
10/01/2018	Document updated with literature review. Coverage unchanged. Reference 6 added.
10/15/2017	Reviewed. No changes.
10/01/2016	New medical document. Reslizumab (CINQAIR®) may be considered medically necessary for add-on maintenance treatment of patients with severe eosinophilic asthma when ALL the following criteria are met: 1) Patient is 18 years and older 2) Patient meets the definition of severe asthma as defined by the following: 12 months of treatment with high-dose inhaled corticosteroid (ICS) in combination with at least one controller medication (e.g., long-acting beta2-agonist [LABA], leukotriene receptor antagonist [LTRA], or theophylline) for the previous year or systemic corticosteroids for 50% or more of the previous year to prevent asthma from becoming uncontrolled or remaining uncontrolled; 3) a pretreatment FEV_1 less than 80% predicted; 4) History of 1 or more exacerbations requiring systemic glucocorticoids while being treated with fluticasone propionate 880µg or more or its equivalent in the last year; AND 5) Patient has eosinophilic phenotype as determined by blood eosinophil count (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection) ≥ 400 cells/µL (See NOTE 1) (within 3 to 4 weeks of

	dosing). NOTE 1: Patients who do not meet the criteria for uncontrolled asthma, but whose asthma worsens on tapering off corticosteroids, will also meet this definition of severe asthma. For definition of uncontrolled asthma see description section. NOTE 1: 1 microliter (µL) is equal to 1 cubic millimeter (mm3). Reslizumab (CINQAIR®) may be considered medically necessary for patients with severe eosinophilic asthma for continuation of therapy after 12 months when treatment has resulted in clinical improvement as documented by one or more of the following: 1) Decreased utilization of rescue medications; OR 2) decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in ICS dose or treatment with systemic corticosteroids); OR 3) Increase in predicted FEV_1 from pretreatment baseline; OR 4) Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing. Reslizumab (CINQAIR®) is considered experimental, investigational and/or unproven when above criteria is not met as outlined and ALL other indications.