LOUISIANA BLUE

reslizumab (Cinqair®)

Policy # 00511
Original Effective Date: 07/20/2016
Current Effective Date: 05/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider reslizumab (Cinqair®)‡ for add-on maintenance treatment of severe asthma (eosinophilic phenotype) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for reslizumab (Cinqair) will be considered for add-on maintenance treatment of severe asthma (eosinophilic phenotype) when the following criteria are met:

Initial Authorization:

I. Cinqair is being used for the treatment of severe asthma (eosinophilic phenotype); AND
II. Patient is greater than or equal to 18 years of age; AND
III. Cinqair is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g., mepolizumab (Nucala®)‡, omalizumab (Xolair®)‡, benralizumab (Fasenra™)‡, dupilumab (Dupixent®)‡]; AND
IV. Cinqair is dosed no higher, or not more often, than 3 mg/kg once every 4 weeks; AND
V. Patient meets ONE of the following (a or b):
    a) Patient has a peripheral blood eosinophil count of ≥ 400 cells per microliter within the previous 4 weeks (prior to treatment with Cinqair); OR
    b) Patient is dependent on systemic corticosteroids; AND
VI. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
    *(Note that the 3 month timeframe is an additional company requirement and will be denied as not medically necessary** if not met)*;
    a) An inhaled corticosteroid (ICS) [e.g., fluticasone products (Arnuity™ Ellipta®, Armonair™ Respiclick®)‡, mometasone products (Asmanex® Twisthaler®, Asmanex HFA)‡, flunisolide products (Aerospan™)‡, ciclesonide products (Alvesco®)‡, budesonide products (Pulmicort Flexhaler®)‡, beclomethasone products (QVAR®)‡]; AND

b) At least ONE of the following (1, 2, 3, OR 4):
   1) Inhaled long-acting beta-agonist (LABA) [e.g., salmeterol products (Serevent® Diskus)‡, olodaterol products (Striverdi® Respimat®)‡, indacaterol products (Arcapta™ Neohaler™)‡]; OR
   NOTE: Use of a combination inhaler containing both an ICS and a LABA would fulfill the requirement for both criteria a.) and b.) [e.g., fluticasone propionate and salmeterol inhalation powder/aerosol (Advair® Diskus/HFA, fluticasone/salmeterol generics, Wixela™ Inhub, AirDuo™ Respiclick)‡, budesonide and formoterol fumarate inhalation aerosol (Symbicort®)‡, fluticasone furoate and vilanterol inhalation powder (Breo® Ellipta)‡, mometasone furoate and formoterol fumarate inhalation aerosol (Dulera®)‡].
   2) Inhaled long-acting muscarinic antagonist (LAMA) [e.g., tiotropium bromide products (Spiriva® Respimat®, Spiriva Handihaler®, Stiolto® Respimat)‡, umeclidinium products (Incruse® Ellipta, Anoro® Ellipta)‡, aclidinium products (Tudorza® Pressair®)‡, glycopyrrolate products (Seebri™ Neohaler, Bevespi™ Aerosphere, Utibron™ Neohaler)‡] OR
   3) Leukotriene receptor antagonist (LTRA) [e.g., montelukast tablets/granules (Singulair®, generics), zafirlukast tablets (Accolate®)]‡; OR
   4) Theophylline (Theo-24, Uniphyl, TheoChron ER, generics); AND

VII. Patient's asthma continues to be uncontrolled as defined by ONE of the following (a, b, c, d, or e):
   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 requiring hospitalization or an Emergency Department (ED) 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's asthma worsens upon tapering of oral corticosteroid therapy; AND

VIII. Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following for at least 4 months of therapy EACH: dupilumab (Dupixent), benralizumab (Fasenra), or mepolizumab (Nucala) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary ** if not met)*

Re-Authorization

Coverage continuation for reslizumab (Cinqair) will be considered for add-on maintenance treatment of severe asthma (eosinophilic phenotype) when the following criteria are met:

I. Patient has received an initial authorization; AND
II. Cinqair is being used for the treatment of severe asthma (eosinophilic phenotype); AND

III. Cinqair is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g. mepolizumab (Nucala), omalizumab (Xolair), benralizumab (Fasenra), dupilumab (Dupixent)]; AND
IV. Patient is greater than or equal to 18 years of age; AND
V. Cinqair is dosed no higher, or not more often, than 3 mg/kg once every 4 weeks; AND
VI. Patient continues to receive the medications required in criterion VI. in the "Initial Criteria"; AND
VII. Patient has responded to Cinqair therapy as determined by the prescribing physician [e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, ED/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy.]
*(Note that this specific patient selection criterion is an additional company requirement and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of reslizumab (Cinqair) when the patient has NOT been on the pre-requisite medications for for the specified amount of time to be **not medically necessary.****

Based on review on available data, the Company considers the continued use of reslizumab (Cinqair) when the patient has NOT responded to Cinqair therapy as determined by the prescribing physician to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of reslizumab (Cinqair) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

Based on review of available data, the Company considers the use of reslizumab (Cinqair) for indications other than the add-on maintenance treatment of severe asthma (eosinophilic phenotype) to be **investigational.***

Background/Overview

Cinqair is an interleukin-5 (IL-5) antagonist monoclonal antibody indicated for add on maintenance treatment of patients with severe asthma aged 18 years of age and older with an eosinophilic phenotype. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Cinqair binds to IL-5 and blocks it from binding to the IL-5

receptor complex on eosinophil surfaces. Inflammation is a large component of asthma and there are multiple cell types and mediators involved. Cinqair reduces the production and survival of eosinophils, however its mechanism of action in asthma has not been definitively established. Cinqair is provided in 100 mg/10 mL (10 mg/mL) single use vials. The recommended dosage regimen is 3 mg/kg once every 4 weeks by intravenous infusion over 20-50 minutes.

Asthma
Asthma is a respiratory disorder characterized by increased responsiveness of the trachea and bronchi to various stimuli resulting in the narrowing of the airways, along with mucous secretion. Symptoms vary in severity and intensity and include wheezing, cough and dyspnea. Attacks can be triggered by exercise, allergens, irritants and viral infections. Based on symptoms, the four levels of asthma severity are:

- Mild intermittent (comes and goes)—you have episodes of asthma symptoms twice a week or less, and you are bothered by symptoms at night twice a month or less; between episodes, however, you have no symptoms and your lung function is normal.
- Mild persistent asthma—you have asthma symptoms more than twice a week, but no more than once in a single day. You are bothered by symptoms at night more than twice a month. You may have asthma attacks that affect your activity.
- Moderate persistent asthma—you have asthma symptoms every day, and you are bothered by nighttime symptoms more than once a week. Asthma attacks may affect your activity.
- Severe persistent asthma—you have symptoms throughout the day on most days, and you are bothered by nighttime symptoms often. In severe asthma, your physical activity is likely to be limited.

Treatment of asthma is based on a step up and step down approach based on the asthma severity and symptoms. Medications include short acting beta agonists for fast relief. Long term treatment centers around the use of ICSs and possible addition of medications such as LABAs, LTRAs, inhaled LAMAs, or theophylline.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Cinqair is an IL-5 antagonist monoclonal antibody indicated for add on maintenance treatment of patients with severe asthma aged 18 years of age and older with an eosinophilic phenotype. Cinqair was approved in March of 2016.

reslizumab (Cinqair®)

Policy # 00511
Original Effective Date: 07/20/2016
Current Effective Date: 05/01/2025

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Cinqair was studied in 4 randomized, double-blind, placebo-controlled studies. There were individuals under 18 years of age involved in the trials, however it is noted in the package insert that Cinqair is not indicated for those under 18 years of age. All subjects continued their background asthma therapy throughout the duration of the studies.

Study 1 included 489 subjects and took place over 52 weeks and compared Cinqair 3 mg/kg IV every 4 weeks versus placebo IV. Subjects in this study had asthma that was inadequately controlled by medium to high dose ICS therapy and they also had blood eosinophils ≥400 cells/microliter. At week 52, subjects receiving Cinqair had a 50% reduction in the frequency of asthma exacerbations compared with placebo (relative risk [RR] 0.50 [95% confidence interval [CI]: 0.37, 0.67]; probability [P]<0.0001).

Study 2 included 464 subjects and was set up similar to Study 1. At week 52, patients receiving Cinqair had a 59% reduction in the frequency of asthma exacerbations compared with placebo (RR 0.41 [95% CI: 0.28, 0.59]; P<0.0001).

Study 3 included 311 subjects and took place over 16 weeks. Subjects were randomized to either Cinqair 0.3 mg/kg IV, Cinqair 3 mg/kg IV or placebo IV every 4 weeks. The subjects had the same clinical characteristics (asthma, eosinophil count) as those in Studies 1 and 2. At week 16, both Cinqair 0.3 mg/kg and Cinqair 3 mg/kg significantly increased FEV1 compared with placebo (treatment differences: +115 mL [95% CI: 0.016, 0.215] and +160 mL [95% CI: 0.060, 0.259], respectively; P = 0.02 and P = 0.0018, respectively).

Study 4 included 492 subjects and took place over 16 weeks. Subjects were randomized to either Cinqair 3mg/kg IV or placebo IV every 4 weeks. The subjects were at least 18 years of age with asthma inadequately controlled by medium to high dose ICS therapy. At week 16, improvements in FEV1 were greater with Cinqair vs. placebo (treatment difference: +76 mL; P = non-significant). In a subgroup of patients with baseline eosinophils ≥ 400 cells/microliter, FEV1 was significantly improved with Cinqair (n = 69) vs. placebo (n = 13) [treatment difference: +270 mL; P = 0.04].

reslizumab (Cinqair®)

Policy # 00511
Original Effective Date: 07/20/2016
Current Effective Date: 05/01/2025

References

1. Cinqair [package insert]. Teva Respiratory, LLC. Frazer, Pennsylvania. Updated 2016.
2. Cinqair Prior Authorization. Express Scripts. Updated 3/30/2016.
3. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3). National Heart, Lung, and Blood Institute. www.nhlbi.nih.gov/guidelines/asthma

Policy History

Original Effective Date: 07/20/2016
Current Effective Date: 05/01/2025

06/30/2016	Medical Policy Committee review
07/20/2016	Medical Policy Implementation Committee approval. New Policy.
10/01/2016	Coding update
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes and HCPCS code update
07/06/2017	Medical Policy Committee review
07/19/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/05/2018	Medical Policy Committee review
07/11/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/03/2019	Medical Policy Committee review
07/18/2019	Medical Policy Implementation Committee approval. Added Dupixent and Fasenra as drugs that can't be used in combination with Cinqair.
07/02/2020	Medical Policy Committee review
07/08/2020	Medical Policy Implementation Committee approval. Updated inhalers within the criteria.
07/01/2021	Medical Policy Committee review
07/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/02/2024	Medical Policy Committee review
05/08/2024	Medical Policy Implementation Committee approval. Updated criteria to require patients to be corticosteroid dependent if the eosinophil count is not >=150 cells/µL. Removed mention of Flovent from policy.

reslizumab (Cinqair®)

Policy # 00511
Original Effective Date: 07/20/2016
Current Effective Date: 05/01/2025

02/06/2025 Medical Policy Committee review
02/12/2025 Medical Policy Implementation Committee approval. Added a requirement to try and fail two of the following medications: Dupixent, Fasenra, or Nucala to the patient selection criteria.
Next Scheduled Review Date: 02/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2786
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.