

09-J2000-63

Original Effective Date: 06/15/16

Reviewed: 01/10/24

Revised: 02/15/24

Subject: Reslizumab (Cinqair®) IV infusion

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Reslizumab (Cinqair), an interleukin-5 antagonist, was approved by the U.S. Food and Drug Administration (FDA) in March 2016 for add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. Reslizumab is not indicated for treatment of other eosinophilic conditions or relief of acute bronchospasm or status asthmaticus.

The safety and efficacy of reslizumab were evaluated in 2 randomized, double-blind, placebo-controlled studies (Studies I, II) 16 to 52 weeks in duration involving 953 patients age 12 years and older with asthma who were required to have a blood eosinophil count of at least 400/mcL (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-high dose inhaled corticosteroids 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. Reslizumab 3 mg/kg administered once every 4 weeks for a total of 13 doses was evaluated compared with placebo.

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.

In Studies I and II, reslizumab significantly reduced the annual rate of clinical asthma exacerbations compared with placebo (0.84 vs 1.81 events per patient/year). One or more exacerbations occurred in 32% of the reslizumab group and 50% of the placebo arm. Reslizumab produced a significantly greater change in FEV1 from baseline to week 16 (0.23 vs 0.11 L). Clinically important changes in patient-reported asthma control scores and quality of life scores were also significantly improved with reslizumab.

Evidence-based practice guidelines or position statements from the American Academy of Allergy, Asthma and Immunology (AAAAI), European Respiratory Society/American Thoracic Society (ERS/ATS), Global Initiative for Chronic Obstructive Lung Disease (GOLD), and National Heart, Lung and Blood Institute (NHLBI) have not been updated to include recommendations surrounding the use of reslizumab.

POSITION STATEMENT:

Site of Care: If reslizumab (Cinqair) is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to [09-J3000-46: Site of Care Policy for Select Specialty Medications](#).

Initiation of reslizumab (Cinqair) meets the definition of **medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with severe eosinophilic asthma
 - a. Member's diagnosis has been confirmed by **ONE** of the following – laboratory documentation must be provided:
 - i. Member has a baseline (prior to therapy with the requested agent) blood eosinophilic count of 150 cells/microliter or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids
 - ii. Member has a fraction of exhaled nitric oxide (FeNO) of 20 parts per billion or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids
 - iii. Member has sputum eosinophils 2% or higher while on highdose inhaled corticosteroids or daily oral corticosteroids
 - b. Member has a history of uncontrolled asthma while on asthma control therapy as demonstrated by **ONE** of the following:
 - i. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months
 - ii. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months
 - iii. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered
 - iv. The member has baseline (prior to therapy with reslizumab) Forced Expiratory Volume (FEV1) that is less than 80% of predicted
 - c. ONE of the following:

- v. The member is **NOT** currently being treated with reslizumab **AND** is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months
- vi. The member is currently being treated with the reslizumab **AND ONE** of the following:
 - Is currently treated with an inhaled corticosteroid for at least 3 months that is adequately dosed to control symptoms
 - Is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months
- vii. The member has an intolerance or hypersensitivity to inhaled corticosteroid therapy
- viii. The member has an FDA labeled contraindication to **ALL** inhaled corticosteroids
- d. ONE of the following:
 - ix. The member is currently being treated for at least 3 months with **ONE** of the following:
 - A long-acting beta-2 agonist (LABA)
 - A leukotriene receptor antagonist (LTRA)
 - Long-acting muscarinic antagonist (LAMA)
 - Theophylline
 - x. The member has an intolerance or hypersensitivity to therapy with LABA, LTRA, LAMA, or theophylline
 - xi. The patient has an FDA labeled contraindication to **ALL** LABA, LTRA, LAMA, **AND** theophylline therapies
- e. Member will continue asthma control therapy in combination with reslizumab
- 2. Reslizumab is prescribed by a board certified (or board eligible) allergist, immunologist, or pulmonologist
- 3. Reslizumab is not used in combination with benralizumab (Fasenra), dupilumab (Dupixent), mepolizumab (Nucala), tezepelumab (Tezspire), or omalizumab (Xolair)
- 4. Dose does not exceed 3 mg/kg every 4 weeks
- 5. Member is 18 years of age or older

Approval duration: 12 months

Continuation of reslizumab (Cinqair) meets the definition of **medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for the treatment of severe eosinophilic asthma, OR the member has previously met all indication-specific initiation criteria
2. Member is currently treated and is compliant with asthma control therapy [e.g, inhaled corticosteroids, ICS/long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA),

long-acting muscarinic antagonist (LAMA), theophylline **AND** has a beneficial response to treatment with reslizumab as indicated by at least **ONE** of the following and supported by documentation from the medical record:

- a. The member has had an increase in percent predicted Forced Expiratory Volume (FEV1)
 - b. The member has had a decrease in the dose of inhaled corticosteroids required to control the patient's asthma
 - c. The member has had a decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma
 - d. The member has had a decrease in number of hospitalizations, need for mechanical ventilation, or visits to urgent care or emergency room due to exacerbations of asthma
3. Reslizumab is prescribed by or in consultation with a board certified (or board eligible) allergist, immunologist, or pulmonologist
 4. Reslizumab is not used in combination with benralizumab (Fasenra), dupilumab (Dupixent), mepolizumab (Nucala), tezepelumab (Tezspire), or omalizumab (Xolair)
 5. Dose does not exceed 3 mg/kg every 4 weeks

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Do not administer as an intravenous push or bolus
- Administer in a healthcare setting by a healthcare professional prepared to manage anaphylaxis
- Recommended dosage regimen is 3 mg/kg once every 4 weeks by intravenous infusion over 20-50 minutes

Dose Adjustments

- None

Drug Availability

- Injection: 100 mg/10 mL (10 mg/mL) solution in single-use vials

PRECAUTIONS:

Boxed Warning

- **Anaphylaxis:** Anaphylaxis has been observed with infusion in 0.3% of patients in placebo-controlled clinical studies. Anaphylaxis was reported as early as the second dose.

Contraindications

- Known hypersensitivity to reslizumab or any of its excipients

Precautions/Warnings

- Malignancy
- Reduction in Corticosteroid Dosage
- Parasitic (Helminth) Infection

BILLING/CODING INFORMATION:

HCPCS Coding

J2786	Injection, reslizumab, 1 mg
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ICD-10 Diagnosis Codes That Support Medical Necessity

J82	Pulmonary eosinophilia, not elsewhere classified
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REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

DEFINITIONS:

FEV1:

Forced expiratory volume in 1 second.

FVC:

Forced vital capacity.

PEF:

Peak expiratory flow.

Mild Intermittent Asthma:

Symptoms < or = to 2 times a week

Asymptomatic and normal PEF between exacerbations
Exacerbations brief (from a few hours to a few days); intensity may vary
Nighttime symptoms < or = to 2 times a month
FEV1 or PEF > or = to 80% predicted
PEF variability < 20%.

Mild Persistent Asthma:

Symptoms > 2 times a week but < 1 time a day
Exacerbations may affect activity
Nighttime symptoms > 2 times a month
FEV1 or PEF > or = to 80% predicted
PEF variability 20 to 30 %.

Moderate Persistent Asthma:

Daily symptoms
Nighttime symptoms > one time a week
Daily use of inhaled short-acting beta2-agonist
Exacerbations may affect activity
Exacerbations > or = to 2 times a week; may last days
FEV1 or PEF > 60% but less than 80% predicted
PEF variability > 30%.

Severe Persistent Asthma:

Continual symptoms (i.e., coughing, dyspnea, wheezing)
Limited physical activity
Frequent exacerbations
Frequent nighttime symptoms
FEV1 or PEF < or = 60% predicted
PEF variability > 30%

RELATED GUIDELINES:

[Benralizumab \(Fasenra\), 09-J2000-92](#)

[Mepolizumab \(Nucala\), 09-J2000-54](#)

[Omalizumab \(Xolair®\), 09-J0000-44](#)

OTHER:

Table 1 - Low, medium and high ICS doses: adults/adolescents (GINA 2020, Box 3-6A)

Inhaled Corticosteroid	Total daily ICS dose (mcg)		
	Low	Medium	High
Beclomethasone dipropionate (pMDI, standard particle, HFA)	200-500	>500-1000	>1000
Beclomethasone dipropionate (pMDI, extrafine particle, HFA)	100-200	>200-400	>400
Budesonide (DPI)	200-400	>400-800	>800
Ciclesonide (pMDI, extrafine particle, HFA)	80-160	>160-320	>320
Fluticasone furoate (DPI)	100	100	200
Fluticasone propionate (DPI)	100-250	>250-500	>500
Fluticasone propionate (pMDI, standard particle, HFA)	100-250	>250-500	>500
Mometasone furoate (DPI)	200	200	400
Mometasone furoate (pMDI, standard particle, HFA)	200-400	200-400	>400

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC)

Table 2 - Low, medium and high ICS doses: children 6-11 years (GINA 2020, Box 3-6B)

Inhaled Corticosteroid	Total daily ICS dose (mcg)		
	Low	Medium	High
Beclomethasone dipropionate (pMDI, standard particle, HFA)	100-200	>200-400	>400
Beclomethasone dipropionate (pMDI, extrafine particle, HFA)	50-100	>100-200	>200
Budesonide (DPI)	100-200	>200-400	>400
Budesonide (nebulas)	250-500	>500-1000	>1000
Ciclesonide (pMDI, extrafine particle, HFA)	80	>80-160	>160
Fluticasone furoate (DPI)	50	50	N/A
Fluticasone propionate (DPI)	50-100	>100-200	>200
Fluticasone propionate (pMDI, standard particle, HFA)	50-100	>100-200	>200
Mometasone furoate (pMDI, standard particle, HFA)	100	100	200

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC)

Table 3 - Low, medium and high ICS doses: children 5 years and younger (GINA 2020, Box 3-6B)

Inhaled Corticosteroid	Total daily ICS dose (mcg)		
	Low	Medium	High
Beclomethasone dipropionate (pMDI, standard particle, HFA)	100-200	>200-400	>400
Beclomethasone dipropionate (pMDI, extrafine particle, HFA)	50-100	>100-200	>200
Budesonide (nebulas)	250-500	>500-1000	>1000
Ciclesonide (pMDI, extrafine particle, HFA)	N/A	N/A	N/A
Fluticasone furoate (DPI)	N/A	N/A	N/A
Fluticasone propionate (pMDI, standard particle, HFA)	100-200	>200-500	>500
Mometasone furoate (pMDI, standard particle, HFA)	100	100	200

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC)

REFERENCES:

1. Akinbami LJ, Moorman JE, Bailey C, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001–2010. National Center for Health Statistics (NCHS) Data Brief No.94; May 2012. Hyattsville, MD: National Center for Health Statistics. Available at: <http://www.cdc.gov/nchs/data/databriefs/db94.htm>. Accessed on November 4, 2015.
2. American Academy of Allergy Asthma and Immunology (AAAAI). AAAAI allergy & asthma medication guide. Available at: <http://www.aaaai.org/conditions-and-treatments/treatments/drug-guide/inhaled-corticosteroids.aspx>. Accessed on September 12, 2015.
3. American Academy of Allergy Asthma and Immunology (AAAAI). Conditions and treatments. Asthma. Available at: <http://www.aaaai.org>. Accessed on November 4, 2015.
4. Assa'ad AH, Gupta SK, Collins MH, et al. An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis. *Gastroenterology*. 2011; 141:1593.
5. Bradding P. Asthma: eosinophil disease, mast cell disease, or both? *Allergy, Asthma, and Clinical Immunology*. 2008; (4) 2:84-90.
6. British Thoracic Society and Scottish Intercollegiate Guidelines Network (BTS/SIGN) national clinical guideline on management of asthma.
7. Castro M, Zangrilli J, Wechsler ME, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet Respir Med*. May 2015;3(5):355-366.
8. Centers for Disease Control and Prevention (CDC). Asthma FastStats. May 2015. Available at: <http://www.cdc.gov/nchs/fastats/asthma.htm>.
9. Chung KF, Wenzel SE, Brozek JL, et al. International European Respiratory Society/American Thoracic Society guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014; 43(2):343-373.
10. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc 2024 [cited 1/1/24]. Available from: <http://www.clinicalpharmacology.com/>.
11. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 1/1/24]. Available from: <http://clinicaltrials.gov/>.
12. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 1/1/24].
13. European Respiratory Society/American Thoracic Society (ERS/ATS) guideline on definition, evaluation, and treatment of severe asthma. *Eur Respir J* 2014 Feb;43(2):343.
14. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention, Global Initiative for Asthma (GINA) 2015. Available at: <http://www.ginasthma.org>. Accessed on November 4, 2015.
15. Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology and Joint Council of Allergy, Asthma and Immunology. Attaining optimal asthma control: a practice parameter. *J Allergy Clin Immunol*. 2005; 116(5):S3-S11.
16. National Asthma Education and Prevention Program (NAEPP). Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. NIH Publication Number 08-5846. Updated August 5, 2008. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>. Accessed on November 4, 2015.
17. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report. *J Allergy Clin Immunol*. 2007 Nov;120(5 Suppl):S94-138.

18. National Heart, Lung and Blood Institute/National Asthma Education and Prevention Program (NHLBI/NAEPP). Guidelines for the Diagnosis and Management of Asthma (EPR-3). 2007. Available here: <http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines>
19. National Heart, Lung, and Blood Institute (NHLBI). National Institutes of Health (NIH). Health information for the public. Lung diseases. Available at: <http://www.nhlbi.nih.gov/health/>. Accessed on November 4, 2015.
20. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 1/1/24]. Available from: <http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/>.
21. Otani IM, Anilkumar AA, Newbury RO, et al. Anti-IL-5 therapy reduces mast cell and IL-9 cell numbers in pediatric patients with eosinophilic esophagitis. *J Allergy Clin Immunol*. 2013; 131(6):1576-1582.
22. 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*. Feb 2012;129(2):456-463, 463 e451-453. PMID.
23. Teva. Cinqair (reslizumab) injection. 2017. [cited 12/3/17]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=053b9158-2a5b-48b9-bf47-5fa78a35ec33>.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/10/24.

GUIDELINE UPDATE INFORMATION:

06/15/16	New Medical Coverage Guideline.
07/15/16	Revision to Position Statement.
10/01/16	Revision: New HCPCS code C9481 added.
01/01/17	Revision: added HCPCS code J2786.
02/15/17	Review and revision; updated references.
02/15/18	Revision to guideline; consisting of position statement, references.
02/15/19	Review and revision; updated references.
11/11/19	Revision to guideline consisting of adding a reference to the Site of Care Policy for Select Specialty Medications and updating the Program Exceptions.
02/15/21	Review and revision; updated position statement, references.
02/15/22	Review and revision; updated position statement, references.
02/15/23	Review and revision; updated position statement, references.
02/15/24	Review and revision; updated position statement, references.