09-J2000-63

Original Effective Date: 06/15/16

Reviewed: 01/08/25

Revised: 02/15/25

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.

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 **AND** has been adherent for 90 days within the past 120 days

vi. The member is currently being treated with the reslizumab **AND ONE** of the following:

- The member is currently treated with an inhaled corticosteroid for at least 3 months **AND** has been adherent for 90 days within the past 120 days that is adequately dosed to control symptoms
- The member is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months **AND** has been adherent for 90 days within the past 120 days

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 **AND** has been adherent for 90 days within the past 120 days 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. **ONE** of the following:

i. The member has tried and had an inadequate response to both benralizumab (Fasenra) **AND** mepolizumab (Nucala) after at least a 3-month trial of each product – documentation from the medical record must be provided

ii. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to both benralizumab (Fasenra) **AND** mepolizumab (Nucala) – documentation from the medical record must be provided

iii. The member has an FDA labeled contraindication to both benralizumab (Fasenra) **AND** mepolizumab (Nucala) – documentation from the medical record must be provided

f. 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: 6 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

ICD-10 Diagnosis Codes That Support Medical Necessity

J82	Pulmonary eosinophilia, not elsewhere classified

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 (nebules)	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 (nebules)	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)			

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/08/25.

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	Revison 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.
02/15/25	Review and revision; updated position statement, references.