09-J2000-63

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Subject: Reslizumab (Cinqair®) IV infusion

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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:

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
2. Member's FEV1 is less than 80% of the predicted value
3. Member's symptoms remain uncontrolled or inadequately controlled despite treatment with at least ONE of the following:
    a. 12 months of high-dose inhaled corticosteroids (see table 1) used in combination with a long-acting beta agonist (e.g., formoterol fumarate (Foradil), salmeterol xinafoate (Serevent)) for a minimum of 3 months
    b. 12 months of high-dose inhaled corticosteroids (see table 1) used in combination with a leukotriene modifier (e.g., montelukast, zafirlukast) for a minimum of 3 months
    c. 12 months of high-dose inhaled corticosteroids (see table 1) used in combination with theophylline for a minimum of 3 months
    d. 6 months of high-dose inhaled corticosteroids (see table 1) with daily oral corticosteroids used in combination with at least one additional controller medication (i.e., long-acting beta agonist, leukotriene modifier, theophylline) for a minimum of 3 months
4. Member has a history of two or more exacerbations requiring systemic glucocorticoids while being treated with a high-dose inhaled corticosteroid in the past year
5. Member's eosinophil count is at least 150 cells/microliter during the previous six weeks OR at least 300 cells/microliter during the previous year – laboratory documentation must be provided
6. Reslizumab is prescribed by a board certified (or board eligible) allergist, immunologist, or pulmonologist
7. Reslizumab is not used in combination with benralizumab (Fasenra), mepolizumab (Nucala) or omalizumab (Xolair)
8. Dose does not exceed 3 mg/kg every 4 weeks
9. 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 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. Decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in inhaled corticosteroid dose or treatment with systemic corticosteroids)
    b. Increase in predicted FEV1 from pretreatment baseline
    c. Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing
3. Reslizumab is not used in combination with benralizumab (Fasenra), mepolizumab (Nucala) or omalizumab (Xolair)
4. 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:

The following codes may be used to describe:

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.

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
Definition of high daily dose of various inhaled corticosteroids in relation to patient age

Inhaled corticosteroid	**Threshold daily dose in mcg considered as high**	
	Age 6–12 years	**Age >12 years**
Beclomethasone dipropionate	≥ 800 (DPI or CFC MDI)	≥ 2000 (DPI or CFC MDI)
	≥ 320 (HFA MDI)	≥ 1000 (HFA MDI)

Budesonide	≥ 800 (MDI or DPI)	≥ 1600 (MDI or DPI)
Ciclesonide	≥ 160 (HFA MDI)	≥ 320 (HFA MDI)
Fluticasone propionate	≥ 500 (HFA MDI or DPI)	≥ 1000 (HFA MDI or DPI)
Mometasone furoate	≥ 500 (DPI)	≥ 800 (DPI)
Triamcinolone acetonide	≥ 1200	≥ 2000
Notes: 1) Designation of high doses is provided from manufacturers' recommendations where possible. 2) As chlorofluorocarbon (CFC) preparations are being taken from the market, medication inserts for hydrofluoroalkane (HFA) preparations should be carefully reviewed by the clinician for the equivalent correct dosage. DPI: dry powder inhaler; MDI: metered-dose inhaler		

REFERENCES:

1. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2019 [cited 1/1/19]. In: STAT! Ref Online Electronic Medical Library [Internet]. Available from: http://online.statref.com/.
2. 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.
3. 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
4. American Academy of Allergy Asthma and Immunology (AAAAI). Conditions and treatments. Asthma. Available at: http://www.aaaai.org. Accessed on November 4, 2015.
5. 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.
6. Bradding P. Asthma: eosinophil disease, mast cell disease, or both? Allergy, Asthma, and Clinical Immunology. 2008; (4)2:84-90.
7. British Thoracic Society and Scottish Intercollegiate Guidelines Network (BTS/SIGN) national clinical guideline on management of asthma.
8. 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.
9. Centers for Disease Control and Prevention (CDC). Asthma FastStats. May 2015. Available at: http://www.cdc.gov/nchs/fastats/asthma.htm.
10. 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.
11. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2019 [cited 1/1/19]. Available from: http://www.clinicalpharmacology.com/.
12. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 1/1/19]. Available from: http://clinicaltrials.gov/.
13. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 1/1/19]. Available from: http://www.thomsonhc.com/.
14. 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.

15. 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.
16. 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.
17. 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.
18. 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.
19. 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
20. 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.
21. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 1/1/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
22. 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.
23. 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
24. 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 1/9/19.

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.
2/15/19	Review and revision; updated references.