Interleukin-5 Antagonists

**Description of Procedure or Service**

(Mepolizumab) Nucala®

Mepolizumab (Nucala®) is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype. Mepolizumab (Nucala®) is not indicated for treatment of other eosinophilic conditions and relief of acute bronchospasm or status asthmaticus.

Mepolizumab (Nucala®) is an interleukin-5 antagonist (IgG1 kappa). IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils.

Mepolizumab binds to IL-5 with a dissociation constant of 100 pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation.

Mepolizumab, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of mepolizumab action in asthma has not been definitively established.

(Reslizumab) Cinqair

Reslizumab (Cinqair) is indicated for the add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. Reslizumab (Cinqair) is not indicated for treatment of other eosinophilic conditions and relief of acute bronchospasm or status asthmaticus.

Reslizumab (Cinqair) is an interleukin-5 antagonist (IgG1 kappa). IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils.

Reslizumab (Cinqair) binds to IL-5 with a dissociation constant of 100 pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation.

Reslizumab, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of reslizumab action in asthma has not been definitively established.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***
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Policy

BCBSNC will provide coverage for interleukin-5 antagonists when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Interleukin-5 Antagonists are covered

Initial Coverage Review:
Interleukin-5 Antagonists are considered medically necessary for the treatment of severe eosinophilic asthma when the following criteria are met:

1. For Mepolizumab (Nucala) the individual is 12 years of age or older; for Reslizumab (Cinqair) the individual is 18 years of age or older; AND

2. Symptoms are inadequately controlled with use of either combination therapy:
   a. 12 months of high-dose inhaled corticosteroid (ICS) given in combination with a minimum of 3 months of controller medication (either a long-acting beta2-agonist [LABA], or leukotriene receptor antagonist [LTRA], or theophylline), unless the individual is intolerant of, or has a medical contraindication to these agents; OR
   b. 6 months of ICS with daily oral glucocorticoids given in combination with a minimum of 3 months of controller medication (either a LABA, or LTRA, or theophylline), unless the individual is intolerant of, or has a medical contraindication to these agents; AND

3. Has one of the following blood eosinophil counts (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection):
   a. Greater than or equal to 150 cells/microliter* at initiation of therapy; OR
   b. Greater than or equal to 300 cells/microliter* in the prior 12 months; *Note: 1 microliter (ul) is equal to 1 cubic millimeter (mm3) AND

4. Diagnosis of asthma with a history of 2 or more exacerbations in the previous year despite regular use of high-dose inhaled corticosteroids plus an additional controller(s) with or without oral corticosteroids;

Continuation of therapy after 12 months: Continued therapy after 12 months is considered medically necessary for the treatment of an individual with documented severe eosinophilic asthma when the following criteria are met: Treatment with mepolizumab has resulted in clinical improvement as documented by one or more of the following:

- Decreased utilization of rescue medications; OR
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- Decreased frequency of exacerbations (defined as worsening of asthma that requires an increase in ICS dose or treatment with systemic corticosteroids); OR
- Increase in predicted FEV1 from pretreatment baseline; OR
- Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing.

When Interleukin-5 Antagonists are not covered

Interleukin-5 antagonists are considered investigational and not medically necessary when criteria are not met and for all other conditions, including but not limited to:

- aspirin-exacerbated respiratory disease (AERD)
- atopic dermatitis
- eosinophilic esophagitis
- eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome)
- nasal polyposis
- hypereosinophilic syndromes (other than severe eosinophilic asthma)
- acute bronchospasm
- status asthmaticus
- diagnosis of any non-FDA approved indication (including urticaria and other eosinophilic conditions)

Policy Guidelines

Mepolizumab (Nucala®)

On November 4, 2015, the U.S. Food and Drug Administration approved Mepolizumab (Nucala®) for use with other asthma medicines for the maintenance treatment of asthma in patients age 12 years and older. Mepolizumab (Nucala®) is approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines.

“This approval offers patients with severe asthma an additional therapy when current treatments cannot maintain adequate control of their asthma,” said Badrul Chowdhury, M.D., Ph.D., director of the Division of Pulmonary, Allergy, and Rheumatology Products in the FDA’s Center for Drug Evaluation and Research.

Mepolizumab (Nucala®) is administered once every four weeks by subcutaneous injection by a health care professional into the upper arm, thigh, or abdomen, with prescribed dosing not to exceed 100 mg every 28 days. Mepolizumab (Nucala®) is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in Chinese hamster ovary cells. Mepolizumab reduces severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.

The safety and efficacy of Mepolizumab (Nucala®) were established in three double-blind, randomized, placebo-controlled trials in patients with severe asthma on currently available therapies. Mepolizumab (Nucala®) or a placebo was administered to patients every four weeks as an add-on asthma treatment. Compared with placebo, patients with severe asthma receiving Mepolizumab had fewer exacerbations requiring hospitalization and/or emergency department visits, and a longer time to the first exacerbation. In addition, patients with severe asthma receiving Mepolizumab experienced greater reductions in their daily maintenance oral corticosteroid dose, while maintaining asthma control compared with patients receiving placebo. Treatment with mepolizumab did not result in a significant improvement in lung function, as measured by the volume of air exhaled by patients in one second.
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Mepolizumab is being investigated for use in the treatment of other conditions, including but not limited to, aspirin-exacerbated respiratory disease (AERD), eosinophilic esophagitis (EoE), eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome), and hypereosinophilic syndromes (HES) unresponsive to other treatments. To date, the FDA has not approved mepolizumab for the treatment of any of these conditions.

Reslizumab (Cinqair)
On March 28, 2016, the U.S. Food and Drug Administration approved reslizumab (Cinqair) for use with other asthma medicines for the maintenance treatment of asthma in patients age 18 years and older. Reslizumab (Cinqair) is approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines.

Reslizumab (Cinqair) prescribed dosing of 3mg/kg is administered once every four weeks by intravenous infusion in a clinical setting prepared to manage anaphylaxis. Reslizumab (Cinqair) is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in murine myeloma non-secreting 0 (NS0) cells. Reslizumab (Cinqair) reduces severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.

The safety and efficacy of Reslizumab (Cinqair) were established in four double-blind, randomized, placebo-controlled trials in patients with severe asthma on currently available therapies. Cinqair or a placebo was administered to patients every four weeks as an add-on asthma treatment. Compared with placebo, patients with severe asthma receiving Reslizumab (Cinqair) had fewer asthma attacks, and a longer time to the first attack. In addition, treatment with Reslizumab (Cinqair) resulted in a significant improvement in lung function, as measured by the volume of air exhaled by patients in one second.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: J2182, J2786*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

*For Policy titled, “Mepolizumab (Nucala®)”*


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Senior Medical Director review 2/2016

For Policy titled, “Interleukin-5 Antagonists”


Medical Director review 11/2016

Policy Implementation/Update Information

2/29/16 Original policy issued titled, “Mepolizumab (Nucala®)” with the following policy statement, “BCBSNC will provide coverage for Mepolizumab (Nucala®) when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.” Specialty Matched Consultant Advisory Panel review 2/2016. Senior Medical Director review 2/2016. (td)

4/29/16 Policy title changed from “Mepolizumab (Nucala®)” to “Interleukin-5 Antagonist”. Policy revised to include information and criteria regarding Reslizumab (Cinqair). References updated. Medical Director review on 4/2016. (jd)

9/30/16 Moved dosing information for Nucala and Cinqair from the “When Covered” section to the Policy Guidelines. Under “Billing/Coding” section, deleted code C3999 and added code C9481 for effective date 10/1/16. (jd)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.