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Coverage Policy Number **IP0421**

Benralizumab

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for **Fasenra®** (benralizumab) subcutaneous injection.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Benralizumab (Fasenra) is considered medically necessary when the following are met:

1. **Asthma.** Individual meets **ALL** of the following criteria (A, B, C, D, E, and F):
   A. Individual is 12 years of age or older
   B. Diagnosis of asthma is confirmed by **BOTH** of the following (i and ii):
      i. Pre-bronchodilator FEV1 below the lower limits of normal for age in the setting of reduced FEV1/FVC (usually less than 80% in adults and 90% in children)

ii. Variable expiratory airflow obstruction as documented by **ONE** of the following (a, b or c):
    a. Increase of at least 12% AND 200 mL in FEV1 after the administration of 200 to 400 mcg albuterol or levalbuterol
    b. Increase of at least 12% AND 200 mL in FEV1 from baseline between visits or after 4 weeks of treatment
    c. Positive exercise or bronchial challenge testing

C. Eosinophilic phenotype defined as **EITHER** of the following (i or ii):
    i. Blood eosinophils greater than or equal to 150 cells/mcl within the previous 6 weeks or within 6 weeks prior to treatment with any anti-interleukin-5 therapy (for example, Fasenra, Cinqair or Nucala)
    ii. History of blood eosinophils greater than or equal to 300 cells/mcl
D. Individual has received at least 3 consecutive months of combination therapy with **BOTH** of the following (i and ii):
    i. An inhaled corticosteroid
    ii. At least one additional asthma controller or asthma maintenance medication (for example, inhaled long-acting beta2-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, and theophylline)

    Note: Use of a combination inhaler containing both an inhaled corticosteroid and a long-acting beta2-agonist would fulfill the requirement for both criteria [i] and [ii].
E. Individual has asthma that is uncontrolled or was uncontrolled at baseline as defined by **ONE** of the following (i, ii, iii, or iv):
    i. Poor symptom control as defined by Asthma Control Questionnaire (ACT) consistently greater than 1.5 or Asthma Control Test less than 20
    ii. Individual experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year
    iii. Individual experienced one or more asthma exacerbation(s) requiring hospitalization, an Emergency Department visit, or an urgent care visit in the previous year
    iv. Daily or every other day oral corticosteroids are required to prevent asthma exacerbations

    Note: "Baseline" is defined as prior to receiving any Tezspire, anti-interleukin-5 therapies (i.e., Cinqair, Fasenra, or Nucala), Dupixent, or Xolair.
F. The medication is prescribed by, or in consultation with, an allergist, immunologist, or pulmonologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Benralizumab (Fasenra) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response, including the following:

1. Individual continues to receive therapy with one inhaled corticosteroid OR one inhaled corticosteroid-containing combination

Note: Examples of a beneficial response to Fasenra therapy are decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department/urgent care, or medical clinic visits due to asthma; and decreased requirement for oral corticosteroid therapy.

Authorization Duration

Initial approval duration: up to 12 months.
Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Benralizumab (Fasenra) is considered experimental, investigational or unproven for **ANY** other use including the following (this list may not be all inclusive):

1. **Chronic Obstructive Pulmonary Disease (COPD).** Fasenra is not indicated for the treatment of COPD.[1] One double-blind, placebo-controlled, Phase IIa study (n = 101) evaluated the efficacy and safety of Fasenra in patients 40 to 80 years of age with eosinophilia and moderate to severe COPD.[8] The annualized rate of acute COPD exacerbations was not reduced with Fasenra compared with placebo. Lung function was also not significantly improved with Fasenra vs. placebo. Numerically greater (although non-significant) improvements in exacerbations and lung function were observed with Fasenra vs. placebo in patients with baseline blood eosinophil levels of 200 cells/microliter or more. Two double-blind, placebo-controlled, Phase III studies (GALATHEA and TERRANOVA) also evaluated Fasenra in patients with moderate to very severe COPD (n = 1,120 and n = 1,545 patients, respectively, with eosinophils ≥ 220 cells/mm^3).[9] Following, 56 weeks of therapy, the annualized COPD exacerbation rates were not statistically significantly reduced with Fasenra vs. placebo in either study. Current COPD guidelines from the Global Initiative for Chronic Lung Disease (GOLD) [2021] note the negative data with Fasenra and state that further studies are needed.[10]

2. **Concurrent use of Fasenra with Another Monoclonal Antibody Therapy (i.e., Cinqair, Nucala, Dupixent, Tezspire, Xolair, or Adbry).** The efficacy and safety of Fasenra used in combination with other monoclonal antibody therapies (e.g., Cinqair, Nucala, Tezspire, Xolair or Adbry) has not been established.[1]

3. **Hypereosinophilic Syndrome.** Fasenra is not indicated for the treatment of eosinophilic conditions other than asthma.[1] A small, randomized, double-blind, placebo-controlled, Phase II trial (n = 20) evaluated the efficacy of Fasenra in patients who had platelet-derived growth factor receptor alpha (PDGFRA)-negative hypereosinophilic syndrome with an absolute eosinophil count of 1,000 cells/mm^3.[12] At Week 12, 90% of patients receiving Fasenra (n = 9/10) vs. 30% of patients receiving placebo (n = 3/10) achieved a 50% or greater reduction in the absolute eosinophil count (P = 0.02). Following the randomized phase, all patients received open-label Fasenra 30 mg every 4 weeks. During this time, 74% of patients (n = 14/19) had sustained clinical and hematologic responses for 48 weeks. The 2019 World Health Organization (WHO)-defined eosinophilic disorders update on diagnosis, risk stratification, and management notes that corticosteroids remain the cornerstone of therapy for several forms of hypereosinophilic syndrome.[13] Use of anti-interleukin (IL) -5 approaches for the treatment of hypereosinophilic syndrome remains investigational. In patients who have idiopathic hypereosinophilic syndrome and end organ damage, enrollment into an anti-IL-5/anti-IL-5 receptor antibody clinical trial is recommended as second-line therapy. Similarly, in patients with lymphocyte-variant hypereosinophilic syndrome, enrollment into an anti-IL-5/anti-IL-5 receptor antibody clinical trial is also recommended as second-line therapy. Further investigation is warranted.

4. **Atopic Dermatitis.** Fasenra is not indicated for the treatment of atopic dermatitis.[1]

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0517	Injection, benralizumab, 1 mg

Background

Overview
Fasenra, an interleukin-5 receptor alpha (IL-5Rα)-directed cytolytic monoclonal antibody, is indicated for **severe asthma** as add-on maintenance treatment of patients ≥ 12 years of age who have an eosinophilic phenotype.[1] Limitations of Use: Fasenra is not indicated for the treatment of other eosinophilic conditions or for the relief of acute bronchospasm/status asthmaticus.

Clinical Efficacy
In two pivotal asthma studies, the addition of Fasenra to existing therapy significantly reduced annualized asthma exacerbation rates in patients with baseline blood eosinophil levels ≥ 300 cells/microliter.[2-4] The magnitude of the improvements observed with Fasenra in this patient population were larger than those observed in patients with lower baseline eosinophil levels (e.g., < 150 cells/microliter). Another pivotal study involved adults with severe asthma receiving high-dose inhaled corticosteroid (ICS)/long-acting beta$_2$-agonist (LABA) and chronic oral corticosteroid therapy who had a baseline blood eosinophil level ≥ 150 cells/microliter.[4]

Guidelines
The Global Initiative for Asthma Global Strategy for Asthma Management and Prevention (2022) proposes a step-wise approach to asthma treatment.[5] Fasenra is listed as an option for add-on therapy in patients ≥ 12 years of age with difficult-to-treat, severe eosinophilic asthma (i.e., asthma that cannot be managed by therapy with medium- to high-dose ICS/formoterol [as both maintenance and reliever therapy] or medium- to high-dose ICS/LABA combination therapy with an as needed short-acting beta$_2$-agonist reliever, with or without an additional controller). Higher blood eosinophil levels, more exacerbations in the previous year, adult-onset asthma, nasal polyposis, maintenance corticosteroid requirements, and low lung function may predict a good asthma response to Fasenra.

According to the European Respiratory Society/American Thoracic Society guidelines (2014; updated in 2020), severe asthma is defined as asthma which requires treatment with a high-dose ICS in addition to a second controller medication (and/or systemic corticosteroids) to prevent it from becoming uncontrolled, or asthma which remains uncontrolled despite this therapy.[6,7] Uncontrolled asthma is defined as asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids or asthma that meets one of the following four criteria:

1) Poor symptom control: Asthma Control Questionnaire consistently ≥ 1.5 or Asthma Control Test < 20;
2) Frequent severe exacerbations: two or more bursts of systemic corticosteroids in the previous year;
3) Serious exacerbations: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year;
4) Airflow limitation: forced expiratory volume in 1 second (FEV_1) < 80% predicted after appropriate bronchodilator withholding.

References

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