



Drug Coverage Policy

Effective Date.....09/01/2024

Coverage Policy Number.....IP0421

Policy Title..... Fasenra

Immunologicals – Fasenra

- Fasenra® (benralizumab subcutaneous injection – AstraZeneca)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

OVERVIEW

Fasenra, an interleukin-5 receptor alpha (IL-5R α)-directed cytolytic monoclonal antibody, is indicated for **severe asthma** as add-on maintenance treatment of patients \geq 6 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 \geq 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 beta₂-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 (2023) 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 severe eosinophilic asthma (i.e., patients who continue to experience exacerbations or have poor symptom control despite treatment with a high-dose ICS/long-acting beta₂-agonist [LABA] and who have eosinophilic biomarkers or require therapy with maintenance oral corticosteroids). Of note, guidelines have not been updated since the lower age indication of Fasenra was FDA-approved. Higher blood eosinophil levels, higher number of severe exacerbations in the previous year, adult-onset asthma, nasal polyposis, maintenance oral 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 (FEV₁) $< 80\%$ predicted after appropriate bronchodilator withholding.

Medical Necessity Criteria

Fasenra is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. Asthma. Approve Fasenra for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, and vi):

- i. Patient is ≥ 6 years of age; AND
- ii. Patient has a blood eosinophil level ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to treatment with Fasenra or another monoclonal antibody therapy that may lower blood eosinophil levels; AND

Note: Examples of monoclonal antibody therapies that may lower blood eosinophil levels include Fasenra, Adbry (tralokinumab-ldrm subcutaneous injection), Cinqair (reslizumab intravenous infusion), Dupixent (dupilumab subcutaneous injection), Nucala (mepolizumab subcutaneous injection), Tezspire (tezepelumab-ekko subcutaneous injection), and Xolair (omalizumab subcutaneous injection).

iii. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):

- a) A medium- or high-dose inhaled corticosteroid; AND
- b) At least one additional asthma controller or asthma maintenance medication; AND

Note: Examples of additional asthma controller or asthma maintenance medications are inhaled long-acting beta₂-agonists, inhaled long-acting muscarinic antagonists, and monoclonal antibody therapies for asthma (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire, Xolair). Use of a combination inhaler containing both a medium- or high-dose inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill the requirement for both criteria a and b.

- iv. Patient has a history of ONE of the following (a or b):
 - a) Patient meets BOTH of the following (1 and 2):
 - (1) Patient has a forced expiratory volume in 1 second (FEV₁) < 80% predicted; AND
Note: The reduced FEV₁ should not be due to smoking-related chronic obstructive pulmonary disease.
 - (2) Patient has an FEV₁/forced vital capacity (FVC) < 0.80; OR
 - b) Patient meets ONE of the following (1, 2, 3, 4, or 5):
 - (1) Increase of > 12% and > 200ml in FEV₁ following administration of a standard dose of a short-acting bronchodilator; OR
 - (2) Increase of > 12% and > 200ml in FEV₁ between prescriber visits; OR
 - (3) Increase of > 12% and > 200ml in FEV₁ from baseline to after at least 4 weeks of asthma treatment; OR
 - (4) Positive exercise challenge testing; OR
 - (5) Positive bronchial challenge testing; AND
Note: The above lung function criteria may be met at anytime prior to or during asthma treatment.
Note: Patients 6 to 11 years of age would only be required to have an increase of > 12% in FEV₁ in each of the respective criteria above (i.e., they would not be required to have an increase > 200 mL)
 - v. Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, or c):
Note: "Baseline" is defined as prior to receiving Fasenra or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Fasenra, Cinqair, Dupixent, Nucala, Tezspire, and Xolair.
 - a) Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
 - b) Patient experienced one or more asthma exacerbation(s) requiring a hospitalization, an emergency department visit, or an urgent care visit in the previous year; OR
 - c) Patient has asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND
 - vi. The medication is prescribed by or in consultation with an allergist, immunologist, or pulmonologist.
- B) Patient is Currently Receiving Fasenra.** Approve for 1 year if the patient meets the following (i, ii, and iii):
- i. Patient has already received at least 6 months of therapy with Fasenra; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Fasenra should be considered under criterion 1A (Asthma, Initial Therapy).
 - ii. Patient continues to receive therapy with one inhaled corticosteroid or one inhaled corticosteroid-containing combination inhaler; AND
 - iii. Patient has responded to therapy as determined by the prescriber.
Note: Examples of a 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.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) If the patient weighs < 35 kg, approve the following dosing regimens (i or ii):

- i. 10 mg administered subcutaneously once every 4 weeks for the first 3 doses; OR
 - ii. 10 mg administered subcutaneously once every 8 weeks; OR
- B) If the patient weighs \geq 35 kg, approve the following dosing regimens (i or ii):**
- i. 30 mg administered subcutaneously once every 4 weeks for the first 3 doses; OR
 - ii. 30 mg administered subcutaneously once every 8 weeks.

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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Chronic Obstructive Pulmonary Disease (COPD).** Fasentra 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 Fasentra 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 Fasentra compared with placebo. Lung function was also not significantly improved with Fasentra vs. placebo. Numerically greater (although non-significant) improvements in exacerbations and lung function were observed with Fasentra 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 Fasentra in patients with moderate to very severe COPD (n = 1,120 and n = 1,545 patients, respectively, with eosinophils \geq 220 cells/mm³).⁹ Following, 56 weeks of therapy, the annualized COPD exacerbation rates were not statistically significantly reduced with Fasentra vs. placebo in either study. Current COPD guidelines from the Global Initiative for Chronic Lung Disease (2024) note the negative data with Fasentra and state that further studies are needed.¹⁰
2. **Concurrent use of Fasentra with another Monoclonal Antibody Therapy.** The efficacy and safety of Fasentra used in combination with other monoclonal antibody therapies have not been established.
Note: Monoclonal antibody therapies are Adbry[®] (tralokinumab-ldrm subcutaneous injection), Cinqair[®] (reslizumab intravenous infusion), Dupixent[®] (dupilumab subcutaneous injection), Nucala[®] (mepolizumab subcutaneous injection), Teszpire[®] (tezepelumab-ekko subcutaneous injection), or Xolair[®] (omalizumab subcutaneous injection).
3. **Hypereosinophilic Syndrome.** Fasentra 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 Fasentra in patients who had platelet-derived growth factor receptor alpha (PDGFRA)-negative hypereosinophilic syndrome with an absolute eosinophil count of 1,000 cells/mm³.¹¹ At Week 12, 90% of patients receiving Fasentra (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 Fasentra 30 mg every 4 weeks. During this time, 74% of patients (n = 14/19) had sustained clinical and hematologic responses for 48 weeks. The World Health Organization (WHO) and international consensus classification of eosinophilic disorders

update on diagnosis, risk stratification, and management (2024) acknowledges that Fasenera has been studied in patients with hypereosinophilic syndrome.¹² A Phase III study of Fasenera in this patient population is currently underway, with primary completion anticipated in May 2024. At this time, the WHO notes that Fasenera remains investigational. Available data with Fasenera is discussed, but this therapy continues to be considered investigational.

Coding Information

- 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:

HCPSC Codes	Description
J0517	Injection, benralizumab, 1 mg

References

1. Fasenera® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; April 2024.
2. Bleeker ER, Fitzgerald JM, Chanez P, et al. Efficacy and safety of Fasenera for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β 2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. *Lancet*. 2016;388:2115-2127.
3. Fitzgerald JM, Bleeker ER, Nair P, et al. Benralizumab, an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomized, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2016;388:2128-2141.
4. Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med*. 2017;376(25):2448-2458.
5. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2023. Available at: <http://www.ginasthma.org>. Accessed on: April 9, 2024.
6. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43:343-373.
7. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society Guideline. *Eur Respir J*. 2020;55:1900588.
8. Brightling CE, Bleeker ER, Panettieri RA, et al. Benralizumab for chronic obstructive pulmonary disease and sputum eosinophilia: a randomized, double-blind, placebo-controlled, phase 2a study. *Lancet Respir Med*. 2014;2(11):891-901.
9. Criner GJ, Celli BR, Brightling CE, et al. Benralizumab for the prevention of COPD exacerbations. *N Engl J Med*. 2019;381(11):1023-1034.
10. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2024 report. Global Initiative for Chronic Obstructive Lung Disease, Inc. Available from: <http://goldcopd.org/>. Accessed on April 9, 2024.
11. Kuang FL, Legrand F, Mikiya M, et al. Benralizumab for PDGFRA-negative hypereosinophilic syndrome. *N Engl J Med*. 2019;380(14):1336-1346.
12. Shomali W, Gotlib J. World Health Organization and international consensus classification of eosinophilic disorders: 2024 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2024;99(5):946-968.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p>Policy Name Change: Updated Policy Name from "Benralizumab" to "Immunologicals – Fasentra."</p> <p>Asthma: Age of approval was reduced from ≥ 12 years of age to ≥ 6 years of age. Updated diagnostic criteria requirements for confirmation of asthma. Added dosing information.</p> <p>Authorization Duration: Updated initial therapy duration from 12 months to 6 months</p> <p>Conditions Not Covered: Removed criterion regarding Atopic Dermatitis.</p>	09/01/2024

The policy effective date is in force until updated or retired.

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