

PRIOR AUTHORIZATION POLICY

POLICY: Immunologicals – Fasenra Prior Authorization Policy

- Fasenra® (benralizumab subcutaneous injection – AstraZeneca)

REVIEW DATE: 03/16/2022; selected revision 07/20/2022

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 ≥ 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 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 (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 an ICS/LABA combination 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: FEV₁ $< 80\%$ predicted after appropriate bronchodilator withholding.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Fasenra. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Fasenra as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Fasenra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Fasenra is recommended in those who meet the following criteria:

FDA-Approved Indication

- 1. Asthma.** Approve Fasenra for the duration noted if the patient meets one of the following conditions (A or B):
 - A) Initial Therapy.** Approve for 6 months if the patient meets the following criteria (i, ii, iii, iv, and v):
 - i.** Patient is ≥ 12 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)** An 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, leukotriene receptor antagonists, and monoclonal antibody therapies for asthma (e.g., Cinqair, Dupixent, Fasenra, Nucala, Tezspire, Xolair). Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfil the requirement for both criteria a and b.
 - iv.** Patient has asthma that is uncontrolled or was uncontrolled at baseline as defined by ONE of the following (a, b, c, d, or e):
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 a forced expiratory volume in 1 second (FEV₁) < 80% predicted; OR
 - d)** Patient has an FEV₁/forced vital capacity (FVC) < 0.80; OR

- e) Patient has asthma that worsens upon tapering of oral (systemic) corticosteroid therapy; AND
 - v. 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 criteria (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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Fasenra is not recommended in the following situations:

- 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 \geq 220 cells/mm³).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 (2022) note the negative data with Fasenra and state that further studies are needed.¹⁰
- 2. Concurrent use with Another Monoclonal Antibody Therapy.** The efficacy and safety of Fasenra used in combination with other monoclonal antibody therapies (e.g., Adbry, Cinqair, Dupixent, Nucala, Tezspire, and Xolair) have not been established.
- 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/mm³.¹¹ 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 World Health Organization-defined eosinophilic disorders update on diagnosis, risk stratification, and management (2022) notes that corticosteroids remain first-line therapy for the treatment of

hypereosinophilic syndrome.¹² Available data with Fasenra is discussed, but this therapy continues to be considered investigational.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Fasenra® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; October 2019.
2. Bleecker ER, Fitzgerald JM, Chanez P, et al. Efficacy and safety of Fasenra 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, Bleecker 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 2021. Available at: <http://www.ginasthma.org>. Accessed on: February 23, 2022.
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, Bleecker 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: 2022 report. Global Initiative for Chronic Obstructive Lung Disease, Inc. Available from: <http://goldcopd.org/>. Accessed on February 23, 2022.
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-defined eosinophilic disorders: 2022 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2022;97(1):129-148.