

POLICY: Immunologicals – Fasentra Utilization Management Medical Policy

- Fasentra[®] (benralizumab subcutaneous injection – AstraZeneca)

EFFECTIVE DATE: 1/1/2020**LAST REVISION DATE:** 09/16/2024**COVERAGE CRITERIA FOR:** All UCare Plans

OVERVIEW

Fasentra, an interleukin-5 receptor alpha (IL-5R α)-directed cytolytic monoclonal antibody, is indicated for **severe asthma** as add-on maintenance treatment of patients ≥ 6 years of age who have an eosinophilic phenotype.¹ Limitations of Use: Fasentra 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 Fasentra 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 Fasentra 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 Fasentra 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 Fasentra 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 Fasentra.

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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Fasenra. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the durations 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 (A or B):
 - A) **Initial Therapy.** Approve for 6 months if the patient meets the following (i, ii, iii, iv, and v):
 - 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) 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, and monoclonal antibody therapies for asthma (e.g., Cinqair, Dupixent, Fasentra, Nucala, Tezspire, Xolair). Use of a combination inhaler containing both an inhaled corticosteroid and additional asthma controller/maintenance medication(s) would fulfill 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 Fasentra or another monoclonal antibody therapy for asthma. Examples of monoclonal antibody therapies for asthma include Fasentra, 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 Fasentra.** 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 Fasentra; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Fasentra 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 Fasentra 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):
- a. 10 mg administered subcutaneously once every 4 weeks for the first 3 doses; OR
b. 10 mg administered subcutaneously once every 8 weeks; OR
- B)** If the patient weighs ≥ 35 kg, approve the following dosing regimens (i or ii):
- a. 30 mg administered subcutaneously once every 4 weeks for the first 3 doses; OR
b. 30 mg administered subcutaneously once every 8 weeks.

Conditions Not Recommended for Approval

Coverage of Fasentra is not recommended in the following situations:

- 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 ≥ 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), Tezspire[®] (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 Fasentra has been studied in patients with hypereosinophilic syndrome.¹² A Phase III study of Fasentra in this patient population is currently underway, with primary completion anticipated in May 2024. At this time, the WHO notes that Fasentra remains investigational. Available data with Fasentra 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. Fasentra[®] subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; April 2024.
2. Bleecker ER, Fitzgerald JM, Chanez P, et al. Efficacy and safety of Fasentra 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 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, 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: 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Conditions not recommended for approval: Criteria were updated to clarify that use of Fasentra with another monoclonal antibody therapy is specific to Cinqair, Nucala, Dupixent, Tezspire, Xolair, and Adbry.	03/22/2023

Annual Revision	Asthma: The age of approval was reduced from ≥ 12 years of age to ≥ 6 years of age. Removed leukotriene receptor antagonists as an example of additional asthma controller or asthma maintenance medications. The Dosing criteria were updated to add 10 mg administered subcutaneously (SC) once every 4 weeks for the first three doses or 10 mg administered SC once every 8 weeks for a patient who weighs < 35 kg. The dosing criteria previously in the policy will still apply to a patient who weighs ≥ 35 kg.	04/19/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024