VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Immunologicals – Fasenra Utilization Management Medical Policy
- Fasenra® (benralizumab injection for subcutaneous use – AstraZeneca)

REVIEW DATE: 03/16/2022

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

Two of the Fasenra pivotal trials included patients 12 to 75 years of age with severe asthma not controlled with inhaled corticosteroid (ICS)/long-acting beta$_2$-agonist (LABA) therapy.[2-4] The addition of Fasenra to existing therapy significantly reduced annualized asthma exacerbation rates in patients with baseline blood eosinophil levels ≥ 300 cells/microliter. 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 ICS/LABA and chronic oral corticosteroid (OCS) therapy who had a baseline blood eosinophil level ≥ 150 cells/microliter.[4] At Week 28, significantly more patients receiving Fasenra were able to reduce their OCS dose compared with placebo.

Guidelines

The Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention (2020) 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, and maintenance oral corticosteroids at baseline may predict a good asthma response to Fasenra.

According to the European Respiratory Society (ERS)/American Thoracic Society (ATS) 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: FEV_1 < 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

FDA-Approved Indications

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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 count ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to treatment with any anti-interleukin-5 therapy; AND
Note: Examples of anti-interleukin-5 therapies include Fasenra, Cinqair® (reslizumab injection for intravenous use), and Nucala® (mepolizumab injection for subcutaneous use).

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 beta$_2$-agonists, inhaled long-acting muscarinic antagonists, leukotriene receptor antagonists, anti-interleukin-5 therapies (e.g., Cinqair, Fasenra, Nucala), and theophylline. Use of a combination inhaler containing both an inhaled corticosteroid and a long-acting beta$_2$-agonist 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):

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 hospitalization or an Emergency Department visit in the previous year; OR

c) Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR

d) Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR

e) The patient has asthma that worsens upon tapering of oral corticosteroid therapy; AND

Note: "Baseline" is defined as prior to receiving any Fasenra or other anti-interleukin-5 therapies (i.e., Cinqair or Nucala).

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.

Dosing. Approve the following dosing regimens (A or B):
A) 30 mg administered subcutaneously (SC) once every 4 weeks for the first 3 doses; OR
B) 30 mg administered subcutaneously (SC) once every 8 weeks.

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 ≥ 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 Anti-Interleukin Monoclonal Antibody.** The efficacy and safety of Fasenra used in combination with other anti-interleukin monoclonal antibodies (e.g., Nucala® [mepolizumab injection for subcutaneous use], Cinqair® [reslizumab injection for intravenous use], Dupixent® [dupilumab subcutaneous injection]) have not been established.

3. **Concurrent use of Fasenra with Xolair® (omalizumab injection for subcutaneous use).** Xolair is a recombinant humanized immunoglobulin G (IgG)1κ monoclonal antibody indicated for use in adults and adolescents (aged ≥ 6 years) with moderate to severe persistent asthma and who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with ICSs.[11] Xolair is also indicated for chronic idiopathic urticaria in adults and adolescents 12 years of age and older who remain symptomatic despite H_1 antihistamine treatment and for nasal polyps, as add-on maintenance treatment in patients ≥ 18 years of age with an inadequate response to nasal corticosteroids. The efficacy and safety of Fasenra used in combination with Xolair have not been established.

4. **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.

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

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/17/2021
Annual Revision	No criteria changes.	03/16/2022