

POLICY: Immunologicals – Fasenra™ (benralizumab injection for subcutaneous use – AstraZeneca)

APPROVAL DATE: 02/20/2019

OVERVIEW

Fasenra is indicated for add-on maintenance treatment of patients ≥ 12 years of age with severe asthma who have an eosinophilic phenotype.¹ Fasenra is not indicated for the treatment of other eosinophilic conditions or for the relief of acute bronchospasm/status asthmaticus. Fasenra should be administered as a subcutaneous (SC) injection by a healthcare professional. Fasenra should be administered as a 30 mg subcutaneous (SC) injection once every 4 weeks (Q4W) for the first three doses, followed by 30 mg SC once every 8 weeks (Q8W). Fasenra must be administered by a healthcare professional. Fasenra is an interleukin (IL)-5 receptor alpha-directed cytolytic antagonist monoclonal antibody. It binds directly to the IL-5R α subunit expressed on the surface of eosinophils and basophils, which *in vitro* has been found to facilitate binding to receptors on immune effector cells, such as natural killer (NK) cells. This results in apoptosis of eosinophils and basophils via antibody-dependent cell-mediated cytotoxicity (ADCC).

Clinical Efficacy

The efficacy of Fasenra was established in three randomized, double-blind, placebo-controlled, multicenter pivotal studies.²⁻⁴ Two asthma exacerbation trials included patients 12 to 75 years of age with severe asthma not controlled with inhaled corticosteroid (ICS)/long-acting beta₂-agonist (LABA) therapy. 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). The third pivotal study was an oral corticosteroid (OCS) reduction study involving adults with severe asthma receiving high-dose ICS/LABA and chronic OCS therapy who had a baseline blood eosinophil level ≥ 150 cells/microliter. At Week 28, significantly more patients receiving Fasenra were able to reduce their OCS dose compared with placebo. A 75% reduction from baseline in the median daily OCS dose was observed with Fasenra vs. a 25% reduction with placebo.

Guidelines

The 2018 Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention proposes a step-wise approach to asthma treatment.⁵ For patients with persistent symptoms or exacerbations despite therapy with a medium- to high-dose ICS/long-acting beta₂-agonist (LABA) combination with or without an additional controller, the GINA recommends referral of the patient to a specialist with expertise in the management of severe asthma. Fasenra is listed as an option for add-on therapy in patients ≥ 12 years of age with severe eosinophilic asthma. The GINA also addresses the potential benefit of phenotyping patients with severe asthma into disease categories to guide future treatment decisions. The anti-IL-5 agents, including Fasenra, are listed as potentially beneficial treatments for patients with severe eosinophilic asthma in their respective approved age groups.

According to the European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014), 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 Uncontrolled asthma is defined as asthma that meets one of the following four criteria: poor symptom control; frequent severe exacerbations; serious exacerbations; or airflow limitation. Additionally, patients may also have severe asthma if their asthma worsens upon tapering of corticosteroids.

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(s). 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). 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. 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.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Asthma in Patients with Severe Disease and an Eosinophilic Phenotype.** Approve Fasenra for the duration noted if the patient meets one of the following conditions (A or B):
 - A) **Initial Therapy.** Approve Fasenra for 6 months if the patient meets the following criteria (i, ii, iii, iv and v):
 - i. Patient is ≥ 12 of age; AND
 - ii. Fasenra is prescribed by or in consultation with an allergist, immunologist, or pulmonologist; AND
 - iii. Patient has a blood eosinophil count of ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to treatment with any anti-interleukin (IL)-5 therapy (e.g., Fasenra, Nucala, Cinqair); AND
 - iv. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
 - a) An inhaled corticosteroid (ICS) [e.g., Aerospan, Alvesco, ArmonAir RespiClick, Arnuity Ellipta, Asmanex Twisthaler/HFA, Flovent Diskus/HFA, Pulmicort Flexhaler, Qvar/Qvar RediHaler, budesonide suspension for inhalation {Pulmicort Respules, generics}]; AND
 - b) At least one additional asthma controller/maintenance medication (e.g., a long-acting beta₂-agonist [LABA] {e.g., Serevent Diskus}; an inhaled long-acting muscarinic antagonist [LAMA] {e.g., Spiriva Respimat}; a leukotriene receptor antagonist [LTRA] {e.g., montelukast tablets/granules (Singulair, generics), zafirlukast tablets (Accolate, generics)}; theophylline [e.g., Theo 24, TheoChron ER, generics]); AND

NOTE: An exception to the requirement for a trial of one additional asthma controller/maintenance medication (criterion b) can be made if the patient has already received anti-IL-5 therapy (e.g., Cinqair, Fasenra, Nucala) used concomitantly with an ICS for at least 3 consecutive months.

NOTE: Use of a combination inhaler containing both an ICS and a LABA would fulfil the requirement for both criteria a and b (e.g., Advair Diskus/HFA, AirDuo RespiClick, Breo Ellipta, Dulera, Symbicort).
 - v. Patient's asthma is uncontrolled or was uncontrolled prior to starting any anti-IL therapy (e.g., Cinqair, Fasenra, Nucala) as defined by ONE of the following (a, b, c, d or e):
 - a) The patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
 - b) The patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) 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) The patient's asthma worsens upon tapering of oral corticosteroid therapy; OR
- B) Patients Continuing Fasenra Therapy.** Approve Fasenra for 1 year if the patient meets the following criteria (i, ii, and iii):
- i. The patient has already received at least 6 months of therapy with Fasenra (Note: Patients who have received < 6 months of therapy or those who are restarting therapy with Fasenra should be considered under criterion 1 [Asthma in Patients with Severe Disease and an Eosinophilic Phenotype, Initial Therapy]); AND
 - ii. Patient continues to receive therapy with one inhaled corticosteroid (ICS) or one ICS-containing combination inhaler (e.g., Flovent Diskus/HFA, ArmonAir RespiClick, Arnuity Ellipta, Asmanex Twisthaler/HFA, Aersopan, Alvesco, Pulmicort Flexhaler, budesonide suspension for inhalation [Pulmicort Respules, generics], Qvar/Qvar RediHaler, Advair Diskus/HFA, AirDuo RespiClick, Symbicort, Breo Ellipta, Dulera); AND
 - iii. The patient has responded to Fasenra therapy as determined by the prescribing physician (e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department (ED)/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy).

Dosing. Approve the following dosing regimens:

- 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

Fasenra has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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.⁷ Patients were randomized (1:1) to receive Fasenra 100 mg SC Q4W for three doses, then 100 mg SC Q8W for an additional five doses (total 48 weeks). The annualized rate of acute COPD exacerbations was not reduced with Fasenra compared with placebo (rates of 0.95 and 0.92, respectively). 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.
2. **Concurrent use of Fasenra with Another Anti-Interleukin (IL) Monoclonal Antibody.** The efficacy and safety of Fasenra used in combination with other anti-IL monoclonal antibodies (e.g., Nucala, Cinqair, 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)1 κ monoclonal antibody indicated for use in adults and adolescents (aged \geq 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.⁸ The efficacy and safety of Fasenra used in combination with Xolair have not been established.

4. **Hyper eosinophilic Syndrome (HES), Idiopathic.** Fasenra is not indicated for the treatment of eosinophilic conditions other than asthma.¹ There is one Phase II study underway evaluating the safety and efficacy of Fasenra for reducing eosinophilia in adult patients with HES.⁹ Results are not yet available.
5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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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.
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9. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2019 Feb 13]. Available from: <https://www.clinicaltrials.gov/ct2/results?term=benralizumab&draw=4&rank=25#rowId24>. Search term: benralizumab.

OTHER REFERENCES USED

- Bleecker ER, Wechsler ME, FitzGerald JM, et al. Baseline patient factors impact on the clinical efficacy of benralizumab for severe asthma. *Eur Respir J*. 2018;52(4):1-13.
- FitzGerald JM, Bleecker ER, Menzies-Gow A, et al. Predictors of enhanced response with benralizumab for patients with severe asthma: pooled analysis of the SIROCCO and CALIMA studies. *Lancet Respir Med*. 2018;6(1):51-64.

HISTORY

Type of Revision	Summary of Changes*	Approval Date
New policy	--	09/26/2018
Early Annual Revision	Updated initial therapy criteria for “Asthma in Patients with Severe Disease and an Eosinophilic Phenotype” to more concisely state the previous therapies required. Added the following: NOTE: An exception to the requirement for a trial of one additional asthma controller/maintenance medication (criterion b) can be made if the patient has already received anti-IL-5 therapy (e.g., Cinqair, Fasenra, Nucala) used concomitantly with an ICS for at least 3 consecutive months.	02/20/2019