# benralizumab (Fasenra Pen™)

EOCCO POLICY

## Policy Type: PA/SP  Pharmacy Coverage Policy: EOCCO174

### Description

Benralizumab (Fasenra Pen) is a subcutaneously administered monoclonal antibody (IgG1 Kappa) that antagonizes interleukin-5 (IL-5).

### Length of Authorization

- Initial: Six months
- Renewal: 12 months

### Quantity limits

| Product Name | Dosage Form | Indication | Quantity Limit |
|---|---|---|---|
| benralizumab (Fasenra) | 30 mg/mL autoinjector | Asthma (severe) | Loading: 1 autoinjector/28 days for 3 doses<br><br>Maintenance: 1 autoinjector/56 days |

### Initial Evaluation

I. Benralizumab (Fasenra Pen) may be considered medically necessary when the following criteria below are met:
   A. Member is 12 years of age or older**; AND**
   B. Medication is prescribed by, or in consultation with, a dermatologist or a physician specializing in allergy, pulmonology, immunology, or ENT (ear, nose, throat); **AND**
   C. Must not be used in combination with another monoclonal antibody (e.g., dupilumab, mepolizumab, omalizumab, reslizumab, etc.); **AND**
   D. A diagnosis of **severe asthma** when the following are met:
      1. Member has **SEVERE** asthma as defined by one of the following:
         i. Symptoms throughout the day
         ii. Nighttime awakenings, often 7x/week
         iii. SABA (e.g., albuterol, levalbuterol) use for symptom control occurs several times per day
         iv. Extremely limited normal activities
         v. Lung function (percent predicted FEV1) < 60%
         vi. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma; **AND**

2. Member must have asthma with an eosinophilic phenotype defined as blood eosinophils ≥300 cells/µL within previous 12 months OR ≥150 cells/µL within 6 weeks of dosing; **AND**
3. Member must have two or more exacerbations in the previous year requiring daily oral corticosteroids for at least 3 days (in addition to the regular maintenance therapy defined below); **AND**
4. Member is currently being treated with:
    i. A medium- to high-dose, or maximally tolerated inhaled corticosteroid (ICS) [e.g., budesonide, fluticasone, mometasone]; **AND**
        a. One additional asthma controller medication (e.g., long-acting beta-2 agonist [LABA] {e.g., Serevent Diskus}, long-acting muscarinic antagonist [LAMA] {e.g., Spiriva Respimat }, leukotriene receptor antagonist [e.g., Singular], or theophylline); **OR**
    ii. A maximally tolerated ICS/LABA combination product (e.g., Advair, Airduo, Breo, Dulera, Symbicort); **AND**
5. Background controller medications (e.g., Advair, Airduo, Breo, Dulera, Symbicort) will be continued with the use of benralizumab (Fasenra), unless contraindicated; **AND**
6. Treatment with mepolizumab (Nucala) has been ineffective, contraindicated, or not tolerated

II. Benralizumab (Fasenra) is considered investigational when used for all other conditions, including but not limited to:
    A. Non-severe, non-eosinophilic phenotype asthma
    B. Atopic dermatitis
    C. Eosinophilic gastritis
    D. Exercise-induced asthma
    E. Chronic obstructive pulmonary disease (COPD)
    F. Hypereosinophilic syndrome

## Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Must not be used in combination with another monoclonal antibody (e.g., dupilumab, mepolizumab, omalizumab, reslizumab, etc.); **AND**

IV. Member has exhibited improvement or stability of disease symptoms (e.g., reduced asthma exacerbations, FEV1, reduced systemic corticosteroid requirements, reduced hospitalizations); **AND**

V. Background controller medications (e.g., Advair, Airduo, Breo, Dulera, Symbicort) will be continued with the use of benralizumab (Fasenra), unless contraindicated.

## Supporting Evidence

I. Benralizumab (Fasenra Pen) is indicated as an add-on maintenance treatment for patients 12 years and older with a diagnosis of severe eosinophilic asthma (SEA). It is now available for self-administration via an autoinjector based off one phase III and one phase I trial that was conducted with the primary objective of usability and pharmacokinetic (PK) exposure. These trials demonstrated that the safety and tolerability of benralizumab (Fasenra Pen) was consistent with the established profile of the medication.

II. The provider administered benralizumab (Fasenra), was FDA approved in the setting of severe eosinophilic asthma and was evaluated in one 52-week dose ranging exacerbation trial, three confirmatory randomized, double-blind trials, and one 12-week lung function trial.

A. The 52- week dose ranging exacerbation trial was a phase 2 randomized, double-blind, placebo-controlled trial. Benralizumab (Fasenra) was administered every 4 weeks for 3 doses followed by every 8 weeks thereafter. In the benralizumab (Fasenra) treatment arm, there was a decrease in annual exacerbation rate with 2, 20, and 100 mg (-12% [80% CI: -51, 18), -34% [80% CI: 6, 54], and -29% [80% CI: 10, 44], respectively).

B. The two confirmatory trials were 48 and 52 weeks in duration. The primary outcome was rate of asthma exacerbations in patients with baseline eosinophil counts of ≥300 cells/µL taking both high-dose ICS and LABA. Rates of exacerbation per year in the benralizumab (Fasenra) arm of both trials was 0.74 and 0.73 compared to 1.52 and 1.01 with placebo (Rate Ratio [95% CI: 0.37, 0.64], [95% CI: 0.54, 0.95], respectively).

C. The third confirmatory trial was 28 weeks in duration and evaluated the effects of benralizumab (Fasenra) on reducing the use of maintenance oral corticosteroids (OCS). The primary endpoint was percent reduction from baseline of OCS use during weeks 24 to 28. The median percent reduction from baseline in the benralizumab (Fasenra) arm was 75% compared to 25% in placebo (95% CI: 60, 88).

D. The 12-week lung function trial measured lung function by the change from baseline $FEV_1$ at week 12. The benralizumab (Fasenra) arm showed an increase of 0.057 liters compared to -0.016 liters in placebo (p=0.040)

III. The Global Initiative for Asthma (GINA) 2020 update recommends the addition of respiratory biologics, with respect to their allergic biomarkers, after inadequate asthma control despite good adherence and inhaler technique on maximized Step 4 (medium dose ICS-LABA) or Step 5 (high dose ICS-LABA) therapy. Other controller options for Step 4 include high dose ICS-LABA, add-on tiotropium, or add-on LTRA. Other controller options for Step 5 include add-on anti-IL5 or add-on low dose OCS, though guidelines do note to consider side effects.

## Investigational or Not Medically Necessary Uses

I. Benralizumab (Fasenra) has not been adequately studied for the following conditions and does not have established safety and efficacy in these populations:
   A. Non-severe, non-eosinophilic phenotype asthma
   B. Atopic dermatitis
   C. Eosinophilic gastritis
   D. Exercise-induced asthma
   E. Hypereosinophilic syndrome
   F. Chronic obstructive pulmonary disease (COPD)
      i. A single phase IIa study compared benralizumab to placebo in patients with COPD and showed there was no difference in rates of exacerbations; therefore, there is insufficient evidence in the safety and efficacy of benralizumab (Fasenra) for use in patients with COPD.

## References

1. Fasenra Pen [Prescribing Information]. Wilmington, DE: AstraZeneca LP. Updated October 2019. Accessed Feb 2021.
2. National Asthma Education and Prevention Program (NAEPP). Guidelines for the diagnosis and management of asthma. Expert Panel Report 3. Bethesda, MD: National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI); August 2007.
3. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2020 Update. Available from: http://www.ginasthma.org. Accessed February 2021.
4. Walford HH, Doherty TA. Diagnosis and management of eosinophilic asthma: a US perspective. J Asthma Allergy. 2014; 7: 53–65.
5. Goldman M, Hirsch I, Zangrilli JG, et al. The association between blood eosinophil count and benralizumab efficacy for patients with severe, uncontrolled asthma: subanalyses of the Phase III SIROCCO and CALIMA studies. Curr Med Res Opin. 2017 Sep;33(9):1605-1613. doi: 10.1080/03007995.2017.1347091. Epub 2017 Jul 19.

## Policy Implementation/Update:

| Action and Summary of Changes | Date |
|---|---|
| Updated renewal length of authorization from six months to 12 months. Revised “severe eosinophilic asthma” verbiage “asthma (severe)” in attempts to align with other respiratory biologics policies. For initial criteria: added dupilumab as an example for another monoclonal antibody that must not be used in | 03/2021 |

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|---|---|
| combination; added prescribed by or in consultation with a specialist requirement; added member must have asthma with an eosinophilic phenotype defined as blood eosinophils ≥300 cells/µL within previous 12 months as an "OR" option to existing required ≥150 cells/µL within 6 weeks of dosing; revised verbiage for add-on maintenance treatment requirements to medium- to high-dose, or maximally tolerated ICS and one additional asthma controller medication OR maximally tolerated ICS/LABA combination, added requirement of continued use with background controller medications. For renewal criteria: added "must not be used in combination with another monoclonal antibody"; consolidated list of clinical improvement examples; added continued background controller medications. For supporting evidence: added GINA 2020 guideline recommendations. For investigational or not medically necessary uses: updated verbiage to current policy format. | |
| Policy created | 02/2020 |