benralizumab (Fasenra)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO174

Description

Benralizumab (Fasenra) 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	Indication	Dosage Form	Quantity Limit
benralizumab (Fasenra)	Asthma (severe)	30 mg/mL autoinjector	**Loading**: 1 autoinjector/28 days for 3 doses **Maintenance**: 1 autoinjector/ 56 days
	Eosinophilic granulomatosis with polyangiitis (EGPA)		1 autoinjector/28 days

Initial Evaluation

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

f. Exacerbations requiring oral systemic corticosteroids are generally more frequent and intense relative to moderate asthma; **AND**

iii. 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**

iv. 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**

v. Member is currently being treated with:

a. A medium- to high-dose, or maximally tolerated inhaled corticosteroid (ICS) [e.g., budesonide, fluticasone, mometasone]; **AND**

i. One additional asthma controller medication (e.g., long-acting beta-2 agonist [LABA] {e.g., Striverdi}, long-acting muscarinic antagonist [LAMA] {e.g., Spiriva Respimat}, leukotriene receptor antagonist [e.g., Singular], or theophylline); **OR**

b. A maximally tolerated ICS/LABA combination product (e.g., Advair, Airduo, Breo, Dulera, Symbicort); **AND**

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

vii. Treatment with mepolizumab (Nucala) has been ineffective, contraindicated, or not tolerated; **OR**

2. **Eosinophilic Ganulomatosis with Polyangiitis (EGPA); AND**

i. Member is 18 years of age or older; **AND**

ii. Member has a confirmed diagnosis of EGPA (aka Churg-Strauss Syndrome) as defined by ALL of the following:

a. History or presence of asthma; **AND**

b. Blood eosinophil level 10% or an absolute eosinophil count >1000 cells/mm^3; **AND**

c. TWO or more of the following:

i. Histopathologic evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration or eosinophil rich granulomatous inflammation

ii. Neuropathy

iii. Pulmonary infiltrates

iv. Sinonasal abnormalities

v. Cardiomyopathy

vi. Glomerulonephritis

vii. Alveolar hemorrhage
viii. Palpable purpura
ix. Antineutrophil Cytoplasmic Antibody (ANCA) positivity; **AND**

iii. History of ONE of the following:
   a. At least one confirmed EGPA relapse within the past two years
   b. Failure to attain remission following induction treatment with a standard regimen (e.g., high-dose glucocorticoids with or without immunosuppressive agents [e.g., methotrexate, mycophenolate mofetil, etc.])
   c. Recurrence of EGPA symptoms while tapering oral corticosteroid; **AND**

iv. Member has been on stable doses of concomitant oral corticosteroid therapy for at least 4 weeks (i.e., prednisone or prednisolone at a dose of at least 7.5 mg/day); **AND**

v. Physician has assessed baseline disease severity utilizing an objective measure/tool (e.g., Birmingham Vasculitis Activity Score [BVAS], history of asthma symptoms and/or exacerbations duration of remission or rate of relapses, etc.); **AND**

vi. 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. A diagnosis of one of the following:
- **Asthma (severe); AND**
  i. Member has exhibited improvement or stability of disease symptoms (e.g., reduced asthma exacerbations, FEV1, reduced systemic corticosteroid requirements, reduced hospitalizations); **AND**
  ii. Background controller medications (e.g., Advair, Airduo, Breo, Dulera, Symbicort) will be continued with the use of benralizumab (Fasenra), unless contraindicated; **OR**
- **Eosinophilic Granulomatosis with Polyangiitis (EGPA); AND**
  i. Member has exhibited improvement or stability of disease symptoms as evidenced in one or more of the following:
    1. Member is in remission [defined as a Birmingham Vasculitis Activity Score (BVAS) score=0 and a prednisone/prednisolone daily dose of ≤ 7.5 mg]
    2. Decrease in maintenance dose of systemic corticosteroids
    3. Improvement in BVAS score compared to baseline
    4. Improvement in asthma symptoms or asthma exacerbations
    5. Improvement in duration of remission or decrease in the rate of relapses.

Supporting Evidence

I. Benralizumab (Fasenra Pen) is indicated as an add-on maintenance treatment for patients six years and older with a diagnosis of severe eosinophilic asthma (SEA) and for patients 18 years and older with a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA).

II. Benralizumab (Fasenra Pen) for self-administration via an autoinjector was established based off two 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.

III. There is a lack of evidence supporting treatment with dual use of biologic therapies and a potential for increased risk of side effects.

IV. **Asthma (severe)**
- 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, one 12-week lung function trial, and one 48-week pharmacokinetic and pharmacodynamic trial.
  i. 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).

ii. 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).

iii. 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).

iv. 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)

v. The 48-week, open-label, pharmacokinetic and pharmacodynamic trial (TATE) was conducted in 28 patients ages six to eleven (mean age 9 years; 6-8 years, n=11; 9-11 years n=17; 32% female, White 29%, Asian 32%, Black or African American 29%) with severe asthma, and with an eosinophilic phenotype. PK, PD, and safety profile of benralizumab 10/30 mg in children with severe eosinophilic asthma are consistent with previous reports in adults and adolescents. Both dose/weight groups achieved near-complete depletion of eosinophils and no new safety signals were identified. The trial was not powered to assess efficacy outcomes.

B. Since severe asthma is associated with difficulty managing symptoms, therapy should be prescribed and managed by a pulmonologist or other specialist with expertise in asthma/lung function.

C. The Global Initiative for Asthma (GINA) 2024 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/high dose maintenance ICS-LABA) or Step 5 (add-on LAMA ± high dose maintenance ICS-formoterol) 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-IL5/5R, anti-IgE, anti-IL4Rα, anti-TSLP, azithromycin, or add-on low dose OCS, though guidelines do note to consider side effects.

D. While benralizumab (Fasenra) is approved for use in patients six years of age and older, the self-administered formulation is only approved for use in patients ≥35kg. For those weighing <35kg benralizumab (Fasenra) should be administered by a healthcare provider.

V. **Eosinophilic Granulomatosis with Polyangiitis (EGPA)**

A. Eosinophilic Granulomatosis with Polyangiitis is a rare disease that does not have well defined diagnostic criteria. Expert consensus suggests that diagnosis should consist of objective evidence of vasculitis coupled with clinical considerations; this generally consists

of confirming presence of asthma, blood eosinophilia, and other manifestations, such as chronic rhinosinusitis with nasal polyps, lung infiltrates/obstructive airway disease, glomerulonephritis, cardiomyopathy, neuropathy, gastroenteritis, and purpura. Given the complexities of diagnosing this rare disease, evaluation should involve a specialist.

B. The FDA approval of benralizumab (Fasenra) for the treatment of EGPA was based on a randomized, double-blind, active-controlled, noninferiority, Phase 3 clinical trial (MANDARA) evaluating the safety and efficacy of benralizumab (Fasenra) against mepolizumab (Nucala). Patients enrolled in the trial were age 18 years and older with a diagnosis of EGPA confirmed by the presence of asthma, blood eosinophilia, and at least two other characteristics of EGPA. Patients also were required to have a history of relapsed and/or refractory disease, defined as at least one confirmed EGPA relapse in the previous two years, while receiving oral prednisolone (or equivalent) of ≥7.5 mg/day, failure to attain remission within 6 months prior to baseline visit following induction with treatment with a standard regimen administered for at least 3 months, or recurrent of symptoms of EGPA while tapering oral glucocorticoids within 6 months prior to baseline.
C. The primary endpoint was the proportion of patients achieving remission (defined as a BVAS of 0 or an oral glucocorticoid dose of ≤4mg/day) at weeks 36 and 48. The adjusted percentage of patients with remission at weeks 36 and 48 was 59% in the benralizumab (Fasenra) group and 56% in the mepolizumab (Nucala) group (difference, 3 percentage points; 95% confidence interval [CI], –13 to 18; P = 0.73 for superiority). These results demonstrate noninferiority, but not superiority, of benralizumab (Fasenra) to mepolizumab (Nucala), since the lower bound of 95% confidence interval exceeded the predetermined noninferiority threshold of −25 percentage points and the P value for superiority was greater than 0.05.
D. According to the American College of Rheumatology (ACR)/Vasculitis Foundation (VF) treatment guidelines, treatment approach should be stratified based on severity. For patients with severe (organ-threatening) manifestations, cyclophosphamide and high-dose corticosteroids should be used for remission induction in new-onset or relapsing disease. Methotrexate, azathioprine, mepolizumab, or rituximab should be used for maintenance of remission in relapsing disease. For patients with non-severe manifestations, glucocorticoids in combination with immunosuppressant agents (e.g., methotrexate, azathioprine, mycophenolate mofetil), mepolizumab (Nucala), or high-dose glucocorticoids only (for select patients) can be considered for remission induction in new-onset or relapsing disease, while mepolizumab (Nucala) monotherapy is recommended for maintenance of remission in relapsing disease. Systemic corticosteroids may be used in conjunction with other medications in the maintenance setting, although the goal is to taper off steroids completely.
E. The Birmingham Vasculitis Activity Score (BVAS) is a validated, objective tool for assessment of disease activity in patients with many forms of vasculitis, consisting of a list of items from

nine organ systems that reflect the typical features of active systemic vasculitis. It provides valid and reliable definitions for remission and response to therapy, as well as flare, and has been widely used in clinical trials, including the MANDARA trial. Baseline BVAS score should be documented prior to initiation of benralizumab (Fasenra) to accurately measure response to therapy upon follow-up.

F. The results of the MANDARA trial demonstrated non-inferiority of benralizumab (Fasenra) compared to mepolizumab (Nucala) for achievement of remission and similar rates of adverse events between the medications during the trial period. Therefore, it is reasonable to conclude that these agents provide a comparable level of safety and efficacy. Thus, pending no contraindication to therapy, preferred formulary therapies should be utilized based on cost-effectiveness.

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 [Prescribing Information]. Wilmington, DE: AstraZeneca LP. Updated September 2024. Accessed October 2024.
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. 2024Update. Available from: http://www.ginasthma.org. Accessed June 2024.
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.
6. Wedner HJ, Fujisawa T, Guilbert TW, et al. Benralizumab in children with severe eosinophilic asthma: Pharmacokinetics and long-term safety (TATE study). *Pediatr Allergy Immunol*. 2024;35(3):e14092.

7. Wechsler ME, Nair P, Terrier B, et al. Benralizumab versus Mepolizumab for Eosinophilic Granulomatosis with Polyangiitis. *N Engl J Med*. 2024;390(10):911-921.
8. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. *Arthritis Rheumatol*. 2021;73(8):1366-1383. doi:10.1002/art.41773.
9. Emmi G, Bettiol A, Gelain E, et al. Evidence-Based Guideline for the diagnosis and management of eosinophilic granulomatosis with polyangiitis. *Nat Rev Rheumatol*. 2023;19(6):378-393. doi:10.1038/s41584-023-00958-w.
10. Hellmich B, Sanchez-Alamo B, Schirmer JH, et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. *Ann Rheum Dis*. 2024;83(1):30-47. Published 2024 Jan 2. doi:10.1136/ard-2022-223764.

Related Policies

Policy Name	Disease state
dupilumab (Dupixent)	Asthma (moderate to severe)
	Atopic dermatitis
	Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
	Prurigo Nodularis
	Eosinophilic Esophagitis
	Chronic Obstructive Pulmonary Disease (COPD)
mepolizumab (Nucala)	Asthma (severe)
	Eosinophilic Granulomatosis with Polyangiitis (EGPA)
	Hypereosinophilic Syndrome
	Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
omalizumab (Xolair)	Chronic Idiopathic Urticaria (CIU)
	Allergic Asthma
	Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)
	IgE-Mediated Food Allergy
	Systemic Mastocytosis
reslizumab (Cinqair)	Asthma (severe)
tepezelumab (Tezspire)	Severe Asthma

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated policy to include newly approved eosinophilic granulomatosis with polyangiitis (EGPA) indication	12/2024
Updated policy name to "benralizumab (Fasenra®) as label does not use Fasenra Pen™ to identify the product. Updated QL table to updated standard format. Updated provider administered agents table to include new 10mg/0.5mL dosage form for pediatric patients under 35kg. Updated age criteria and supporting evidence to include the TATE trial for use in pediatric patients six and older. Updated supporting evidence to include GINA 2024 recommendations for the treatment of severe asthma.	7/2024
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 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	03/2021

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