Fasenra (benralizumab) injection, for subcutaneous use

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Related Policies

- N/A

Coverage Rationale

This policy is applicable to Fasenra (benralizumab) injection pre-filled syringe only.

Eosinophilic Granulomatosis with Polyangiitis

For initial coverage of Fasenra (benralizumab) injection for eosinophilic granulomatosis with polyangiitis, the following will be required:

- Diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) **and**
- Patient's disease has relapsed or is refractory to standard of care therapy (i.e., corticosteroid treatment with or without immunosuppressive therapy) **and**
- Patient is currently receiving corticosteroid therapy (e.g., prednisolone, prednisone) unless there is a contraindication or intolerance to corticosteroid therapy **and**
- Prescribed by or in consultation with one of the following:
  - Pulmonologist
  - Rheumatologist
  - Allergist/Immunologist

For reauthorization coverage of Fasenra (benralizumab) injection for eosinophilic granulomatosis with polyangiitis, the following will be required:

- Patient demonstrates positive clinical response to therapy (e.g., increase in remission time)

Hypereosinophilic Syndrome (HES)

For initial coverage of Fasenra (benralizumab) injection for hypereosinophilic syndrome (HES), the following will be required:

- Diagnosis of hypereosinophilic syndrome (HES) **and**

- Patient is 12 years of age or older **and**
- Provider attests that other non-hematologic secondary causes have been ruled out (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy) **and**
- Patient is Fip1-like1-platelet-derived growth factor receptor alpha (FIP1L1-PDGFRA)-negative as detected by an FDA-approved test or a test performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA) **and**
- Patient has uncontrolled HES as evidenced by both of the following:
    - Pre-treatment blood eosinophil count greater than or equal to 1000 cells/microliter **and**
    - One of the following:
        - History of 2 or more flares within the past 12 months **or**
        - Signs or symptoms of active HES flare (e.g., dyspnea) **and**
- Trial (of a minimum 28-day supply) and inadequate response contraindication, or intolerance to one of the following:
    - Corticosteroid therapy (e.g., prednisone) **or**
    - Cytotoxic/immunosuppressive therapy (e.g., hydroxyurea, cyclosporine, imatinib) **and**
- Prescribed by or in consultation with one of the following:
    - Allergist/Immunologist
    - Hematologist

For reauthorization coverage of Fasenra (benralizumab) injection for hypereosinophilic syndrome (HES), the following will be required:

- Patient demonstrates positive clinical response to therapy (e.g., reduction in flares, decreased blood eosinophil count, reduction in corticosteroid dose)

Severe Eosinophilic Asthma

For initial coverage of Fasenra (benralizumab) injection for severe eosinophilic asthma, the following will be required:

- Diagnosis of severe asthma **and**
- Asthma is an eosinophilic phenotype as defined by a baseline (pre-treatment) peripheral blood eosinophil level greater than or equal to 150 cells per microliter **and**
- One of the following:
    - Patient has had at least two or more asthma exacerbations requiring systemic corticosteroids (e.g., prednisone) within the past 12 months **or**
    - Prior asthma-related hospitalization within the past 12 months **and**
- One of the following:
    - Both of the following:
        - Patient is 6 years of age or older but less than 12 years of age **and**
        - Patient is currently being treated with one of the following unless there is a contraindication or intolerance to these medications:
            - Both of the following:
                - Medium-dose inhaled corticosteroid (e.g., greater than 100 – 200 mcg fluticasone propionate equivalent/day)
                - Additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] [e.g., montelukast], long-acting beta-2 agonist [LABA] [e.g., salmeterol], long-acting muscarinic antagonist [LAMA] [e.g., tiotropium]) **or**
            - One medium-dose combination ICS/LABA product (e.g., Advair Diskus [fluticasone propionate 100 mcg/ salmeterol 50 mcg], Symbicort [budesonide 80 mcg/ formoterol 4.5 mcg], Breo Ellipta [fluticasone furoate 50 mcg/ vilanterol 25 mcg]) **or**
    - Both of the following:
        - Patient is 12 years of age or older **and**

        - Patient is currently being treated with one of the following unless there is a contraindication or intolerance to these medications:
            - Both of the following:
                - High-dose inhaled corticosteroid (ICS) (e.g., greater than 500 mcg fluticasone propionate equivalent/day)
                - Additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] [e.g., montelukast], long-acting beta-2 agonist [LABA] [e.g., salmeterol], long-acting muscarinic antagonist [LAMA] [e.g., tiotropium]) **or**
            - One maximally-dosed combination ICS/LABA product (e.g., Advair [fluticasone propionate 500 mcg/ salmeterol 50 mcg], Symbicort [budesonide 160 mcg/ formoterol 4.5 mcg], Breo Ellipta [fluticasone 200mcg/ vilanterol 25mcg]) **and**
- Prescribed by or in consultation with one of the following:
    - Pulmonologist
    - Allergist/Immunologist

For reauthorization coverage of Fasenra (benralizumab) injection for severe eosinophilic asthma, the following will be required:

- Patient demonstrates positive clinical response to therapy (e.g., reduction in exacerbations, improvement in forced expiratory volume in 1 second [FEV1], decreased use of rescue medications) **and**
- Patient continues to be treated with an inhaled corticosteroid (ICS) (e.g., fluticasone, budesonide) with or without additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] [e.g., montelukast], long-acting beta-2 agonist [LABA] [e.g., salmeterol], long-acting muscarinic antagonist [LAMA] [e.g., tiotropium]) unless there is a contraindication or intolerance to these medications **and**
- Prescribed by or in consultation with one of the following:
    - Pulmonologist
    - Allergist/Immunologist

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0517	Injection, benralizumab, 1 mg

ICD-10 Code	Description
D72.11	Hypereosinophilic Syndrome
J45.50	Severe persistent asthma, uncomplicated
J82.81	Eosinophilic pneumonia, NOS
J82.82	Acute eosinophilic pneumonia
J82.83	Eosinophilic asthma
J82.89	Other pulmonary eosinophilia, not elsewhere classified
M30.1	Polyarteritis with lung involvement [EGPA/Churg-Strauss]

Background

Benralizumab is a humanized afucosylated, monoclonal antibody (IgG1, kappa) that directly binds to the alpha subunit of the human interleukin-5 receptor (IL-5Rα). The IL-5 receptor is expressed on the surface of eosinophils and basophils. In an in vitro setting, the absence of fucose in the Fc domain of benralizumab facilitates binding to Fc γ RIII receptors on immune effector cells, such as natural killer (NK) cells, leading to apoptosis of eosinophils and basophils through antibody-dependent cell-mediated cytotoxicity (ADCC). Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation. Benralizumab, by binding to the IL-5Rα chain, reduces eosinophils through ADCC; however, the mechanism of benralizumab action in asthma and EGPA has not been definitively established.

Respiratory and allergy biologics are a mainstay of treatment for severe asthma. Asthma is a chronic lung disease that inflames and narrows the airways, making it difficult to breathe. Asthma causes recurring periods of wheezing, chest tightness, shortness of breath, and coughing. In 2022, asthma affected an estimated 22 million adults and 4.5 million children in the United States (U.S.) (Centers for Disease Control and Prevention Web site 2024). Current pharmacologic options for asthma management are categorized as: (1) controller medications to achieve and maintain control of persistent asthma or prevent exacerbations, and (2) reliever medications for symptom relief and before exercise to prevent exercise-induced asthma symptoms (Cloutier et al 2020, NHLBI 2007, Global Initiative for Asthma [GINA] 2025). Severe asthma is defined as asthma that is uncontrolled despite adherence to maximal optimized high-dose ICS/LABA treatment or asthma that requires high doses of ICS/LABA to remain controlled (GINA 2025).

EGPA, previously called Churg-Strauss syndrome, is a systemic necrotizing vasculitis that affects small-to-medium-sized vessels. It is typically associated with eosinophilia and severe asthma (Chung et al 2021, Connelly-Smith et al 2023, Groh et al 2015). EGPA is a rare condition with a prevalence of approximately 13 cases per 1 million persons and an annual incidence of approximately 7 new cases per 1 million persons. It has a higher incidence in patients with asthma (Groh et al 2015).

Hypereosinophilic Syndromes (HES) are disorders characterized by the overproduction of eosinophils, which causes organ damage (Roufosse et al 2025). Treatment for idiopathic HES may include systemic glucocorticoids, imatinib, hydroxyurea, interferon alfa, alemtuzumab, and Janus kinase inhibitors (e.g., tofacitinib and ruxolitinib). Mepolizumab was FDA-approved for HES in 2020, and benralizumab was approved in 2026.

Clinical Evidence

Asthma

The safety and efficacy of benralizumab were evaluated in a 52-week dose-ranging exacerbation trial, 4 confirmatory trials, and a 12-week lung function trial (Bleecker et al 2016, Castro et al 2014, Ferguson et al 2017, Fitzgerald et al 2016, Nair et al 2017, Harrison et al 2021).

- SIROCCO was a randomized, multicenter, double-blind, placebo-controlled, 48-week, Phase 3 trial (N = 1205) involving patients with severe asthma with eosinophilia uncontrolled with high-dose ICS and LABAs (Bleecker et al 2016). Enrolled patients were randomly assigned to placebo (n = 407), benralizumab 30 mg every 4 weeks (n = 400), or benralizumab 30 mg every 8 weeks (n = 398). Compared with placebo, benralizumab reduced the annual asthma exacerbation rate over 48 weeks when administered every 4 weeks (RR, 0.55; 95% CI, 0.42 to 0.71; $p < 0.0001$) or every 8 weeks (RR, 0.49; 95% CI, 0.37 to 0.64; $p < 0.0001$). Both doses of benralizumab also significantly improved pre-bronchodilator FEV1 in patients at week 48 vs placebo. Asthma symptoms were improved with benralizumab every 8 weeks, but not every 4 weeks, as compared to placebo.
- CALIMA was a randomized, multicenter, double-blind, placebo-controlled, 56-week, Phase 3 trial that assessed benralizumab as add-on therapy (to high-dose ICS and LABA) for patients with severe, uncontrolled asthma and elevated blood eosinophil counts (Fitzgerald et al 2016). A total of 1306 patients were randomly assigned to

benralizumab 30 mg every 4 weeks (n = 425), benralizumab 30 mg every 8 weeks (n = 441) or placebo (n = 440). When compared to placebo, significant reductions in annual exacerbation rates were seen with benralizumab every 4 weeks (RR, 0.64; 95% CI, 0.49 to 0.85; p = 0.0018) and every 8 weeks (RR, 0.72; 95% CI, 0.54 to 0.95; p = 0.0188). Benralizumab was also associated with significantly improved pre-bronchodilator FEV1 and total asthma symptom scores vs placebo.

- Fitzgerald et al conducted a study exploring the efficacy of benralizumab for patients with different baseline blood eosinophil thresholds and exacerbation histories. This study was a pooled analysis (n = 2295 patients) of the results from the SIROCCO and CALIMA Phase 3 studies. The annual exacerbation rate among patients with baseline blood eosinophil counts of ≥ 0 cells/ μ L was 1.16 (95% CI, 1.05 to 1.28) in patients who received placebo vs 0.75 (0.66 to 0.84) in patients who received benralizumab every 8 weeks (RR, 0.64; 0.55 to 0.75; p < 0.0001). In patients who received benralizumab every 4 weeks who had eosinophil counts of ≥ 0 cells/ μ L, the annual exacerbation rate was 0.73 (0.65 to 0.82); RR vs placebo was 0.63 (0.54 to 0.74; p < 0.0001). Greater improvements in the annual exacerbation rate were seen with benralizumab compared with placebo for patients with a combination of high blood eosinophil thresholds and a history of more frequent exacerbations (Fitzgerald et al 2018).
- The effectiveness of Fasenra in pediatric patients 6 to 11 years of age is extrapolated from efficacy in three clinical trials (SIROCCO, CALIMA, and ZONDA) with support from pharmacokinetic analysis and pharmacodynamic response in pediatric patients aged 6 to 11 years compared to adults and adolescents (Fasenra prescribing information 2024). TATE is a 48-week, open-label, pharmacokinetic and pharmacodynamic trial that was conducted in 28 patients aged 6 to 11 years (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. Based upon the pharmacokinetic data from TATE, a subcutaneous dose of 10 mg (patients <35 kg) and subcutaneous dose of 30 mg (patients ≥35 kg) of benralizumab administered every 4 weeks for the first 3 doses, then every 8 weeks thereafter in patients aged 6 to 11 years was determined to have similar or higher exposure, respectively, to adults and adolescents administered a subcutaneous dose of 30 mg with the same dosing regimen. The pharmacodynamic response observed in TATE for pediatric patients aged 6 to 11 years was similar to that observed in adults and adolescents. No new safety signals were observed from TATE and safety for the higher drug exposure is supported by safety data from SIROCCO and CALIMA in adults and adolescents, and ZONDA in adults, who received 30 mg of FASENRA every 4 weeks for 1 year.

EGPA

MANDARA was a Phase 3, multicenter, double-blind, active-controlled noninferiority trial comparing the efficacy of benralizumab vs mepolizumab in 140 adult patients with relapsing or refractory EGPA. For the primary endpoint, the adjusted proportion of patients with remission at weeks 36 and 48 was 59% in patients treated with benralizumab vs 56% with mepolizumab (difference, 3%; 95% CI, -13 to 18; p = 0.73), demonstrating the noninferiority of benralizumab to mepolizumab. For secondary endpoints, the accrued duration of remission and time to first relapse were similar between agents, and complete withdrawal of corticosteroids during weeks 48 to 52 was achieved in 41% of patients taking benralizumab and 26% of patients taking mepolizumab (Wechsler et al 2024).

HES

The safety and efficacy of benralizumab for hypereosinophilic syndrome (HES) were evaluated in the Phase 3 NATRON trial, a randomized, double-blind, placebo-controlled study in patients aged 12 years and older with recurrent or active HES, in which benralizumab significantly reduced HES flares compared with placebo (Ogbogu et al. 2026).

- NATRON was a Phase 3, randomized, double-blind, parallel -group, placebo-controlled clinical trial with a treatment duration of 24 weeks, in patients aged 12 years and older. A total of 133 adult and pediatric patients who had signs or symptoms of HES flare or had experienced at least 2 HES flares within the past 12 months received randomized treatment. At screening, patients had a blood eosinophil count ≥1,000 cells/µL and had been on stable HES therapy (which could include OCS, immunosuppressive/cytotoxic therapy) for at least 4 weeks. Patients with non-hematologic secondary HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy) or patients who were FIP1L1-PDGFRA kinase-positive were excluded

from the study. Patients were randomized to receive FASENRA 30 mg or placebo administered subcutaneously every 4 weeks while continuing their stable HES therapy

- The efficacy of FASENRA in HES was established based upon time to first HES flare and the proportion of patients who experienced a HES flare during the 24-week treatment period. An HES flare was defined as an HES clinical manifestation or laboratory abnormality resulting in one of the following: an increase in or addition of OCS at a dosage of 10 mg/day or more for at least 2 days; an increase in or addition of new cytotoxic and/or immunosuppressive HES therapy; or hospitalization.
- Over the 24-week treatment period, treatment with FASENRA delayed the time to first HES flare and resulted in a significant 65% reduction in the risk of first flare versus placebo (HR, 0.35; 95% CI, 0.18 to 0.69; p = 0.0024).
- Treatment with FASENRA resulted in a 52% relative reduction in the proportion of patients who experienced a HES flare and significantly reduced the number of HES flares observed during the treatment period (Table 10). In addition, fewer patients experienced HES flares resulting in an increased use of OCS with FASENRA (12 [18%]) compared to placebo (28 [42%]) over the 24-week treatment period.
- Fatigue-related symptoms and impacts were evaluated using the Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue Short Form 7a, with scores ranging from 0 to 100 and higher scores indicating greater fatigue. Compared to placebo, treatment with FASENRA resulted in a statistically significant reduction in fatigue-related symptoms and impacts at Week 24 (p=0.0017). The LS mean absolute change from baseline in PROMIS Fatigue Short Form 7a score at Week 24 was -8.6 (95% CI: -10.6 to -6.6; baseline mean 54.3) in the FASENRA group and -3.9 (95% CI: -6.0 to -1.8; baseline mean 55.9) in the placebo group.

Clinical Guidelines

Asthma

The National Asthma Education and Prevention Program (NAEPP) guideline from the NHLBI states that the initial treatment of asthma should correspond to the appropriate asthma severity category, and it provides a stepwise approach to asthma management. Long-term control medications such as ICSs, long-acting bronchodilators, leukotriene modifiers, cromolyn, and immunomodulators should be taken daily on a long-term basis to achieve and maintain control of persistent asthma. ICSs are the most potent and consistently effective long-term asthma control medication. Quick-relief medications such as SABAs and anticholinergics are used to provide prompt relief of bronchoconstriction and accompanying acute symptoms such as cough, chest tightness, and wheezing. Systemic corticosteroids are important in the treatment of moderate or severe exacerbations because these medications prevent progression of the exacerbation, speed recovery, and prevent relapses (NHLBI 2007). A 2020 focused update of the 2007 NAEPP guideline has provided additional updated recommendations on the use of intermittent ICSs and the use of LAMAs as add-on therapy (Cloutier et al 2020).

The 2025 GINA report also provides a stepwise approach to asthma management (GINA 2025). Treatment recommendations are based on patient age, and stepping down should be considered when asthma symptoms have been well-controlled and lung function have been stable for ≥ 2 to 3 months. ICS/beta2-agonist combination products are recommended for both controller (i.e., maintenance treatment) and reliever use in patients ≥ 6 years of age, while the preferred controller option in patients ≤ 5 years of age consists of low-dose ICS for Step 2 and double low-dose ICS for Step 3, with a specialist assessment recommended for Step 4 if a patient's asthma is not well-controlled on double low-dose ICS. In patients ≥ 6 years of age diagnosed with severe asthma and uncontrolled on Step 4 treatment, phenotyping for Type 2 inflammation into categories such as severe allergic, aspirin-exacerbated, allergic bronchopulmonary aspergillosis, chronic rhinosinusitis, nasal polyposis, atopic dermatitis, or eosinophilic asthma is recommended. Add-on treatment with a biologic agent should be considered as follows:

- Severe allergic asthma: Anti-IgE treatment with omalizumab is recommended for patients ≥ 6 years of age.
- Severe eosinophilic asthma: Add-on anti-IL-5 therapy is recommended for patients ≥ 6 years of age (mepolizumab and benralizumab) or ≥ 18 years of age (reslizumab).
- Severe eosinophilic/Type 2 asthma: Anti IL4 therapy (dupilumab) is recommended for patients ≥ 6 years of age.
- Adults or adolescents requiring oral corticosteroids for maintenance therapy: Anti IL4 therapy (dupilumab) is recommended.

- Severe asthma: Anti-TSLP therapy (tezepelumab-ekko) is recommended for patients ≥ 12 years of age.
- Prior to initiation of a biologic agent, several factors should be considered including cost, insurance eligibility criteria, evaluation of predictors of response, delivery route, dosing frequency, and patient preference.

The European Respiratory Society/American Thoracic Society guideline on the management of severe asthma suggests the use of anti-IL-5 therapy as an add-on in adults with severe uncontrolled eosinophilic asthma or severe corticosteroid-dependent asthma. A blood eosinophil count of ≥ 150 cells/µL is suggested as a cut-point to guide initiation of anti-IL-5 therapy in adults with severe asthma and prior exacerbations. A blood eosinophil count of ≥ 260 cells/µL or an exhaled nitric oxide level of 19.5 parts per billion or greater may be used to identify adolescents and adults with severe allergic asthma who are likely to benefit from anti-IgE treatment (Holguin et al 2020).

The American College of Chest Physicians (ACCP) also developed a guideline addressing biologic management in adults with severe asthma. For adults with moderate to severe allergic asthma and ≥ 1 exacerbation per year requiring OCS, the panel recommends treatment with either omalizumab or dupilumab, using individual clinical characteristics to guide selection. For severe, steroid-dependent asthma, the panel recommends either anti-IL-5/IL-5 receptor alpha (IL-5R α) therapy or dupilumab and recommends dupilumab over tezepelumab-ekko. For moderate to severe asthma that does not demonstrate a clinical response to omalizumab after 4 to 6 months, the panel recommends switching to either anti-IL-5/IL-5R α therapy or dupilumab. For severe asthma that does not respond to anti-IL-5/IL-5R α therapy after 4 to 6 months, the panel recommends either dupilumab or tezepelumab-ekko, with dupilumab preferred in those who are steroid dependent. For those who do not respond to dupilumab after 4 to 6 months, the panel recommends either anti-IL-5/IL-5R α therapy or tezepelumab-ekko, with anti-IL-5/IL-5R α therapy preferred in steroid-dependent patients. Finally, for those with severe asthma receiving anti-IL-5/IL-5R α therapy who have not demonstrated a clinical response by 4 to 6 months, the panel recommends using a post-treatment FeNO ≥25 ppb to guide switching to dupilumab. All recommendations carry a conditional strength of recommendation and are based primarily on very low-certainty evidence (Oberle et al 2026).

EGPA

In 2023, a European guideline developed by a panel of multidisciplinary experts provided recommendations for the diagnosis and management of EGPA. For remission maintenance in patients with severe EGPA, the panel recommended the use of rituximab, mepolizumab, or traditional disease-modifying therapies in combination with glucocorticoids. In patients with non-severe EGPA, the panel suggested treatment with glucocorticoids, either alone or in combination with mepolizumab. Glucocorticoids should be tapered to the minimum effective dosage to reduce toxicity. Key efficacy trials with benralizumab in patients with EGPA were published after these guidelines; benralizumab is recommended only for consideration in patients with disease refractory to mepolizumab (Emmi et al 2023).

In 2021, a joint guideline from the American College of Rheumatology and Vasculitis Foundation published recommendations for the management of EGPA along with other related conditions (Chung et al 2021). The following relevant conditional recommendations were provided:

- Patients with active, severe EGPA should be treated with cyclophosphamide or rituximab over mepolizumab for remission induction.
- Patients with active, non-severe EGPA should be treated with mepolizumab and glucocorticoids over methotrexate, azathioprine, or mycophenolate mofetil and glucocorticoids.
- Patients with severe EGPA whose disease has entered remission should be treated with methotrexate, azathioprine, or mycophenolate mofetil over mepolizumab for remission maintenance.
- Patients with EGPA who have experienced relapse with non-severe disease manifestations (i.e., asthma and/or sinonasal disease) while receiving methotrexate, azathioprine, or mycophenolate mofetil: mepolizumab should be added over switching to another agent.
- Patients with EGPA who have experienced relapse with non-severe disease manifestations (asthma and/or sinonasal disease) while receiving low-dose glucocorticoids and no other therapy: mepolizumab should be added over adding methotrexate, azathioprine, or mycophenolate mofetil.

- Patients with EGPA and high serum IgE levels who have experienced relapse with non-severe disease manifestations (asthma and/or sinonasal disease) while receiving methotrexate, azathioprine, or mycophenolate mofetil: mepolizumab should be added over adding omalizumab.

Both the EGPA (Churg-Strauss) Consensus Task Force recommendations and the American Society for Apheresis guideline recommend glucocorticoids alone for patients without life- and/or organ-threatening EGPA. For patients with life- and/or organ-threatening EGPA, both glucocorticoids and an immunosuppressant are recommended, as well as maintenance therapy with azathioprine or methotrexate. Guidelines from the American Society for Apheresis recognized mepolizumab as a future treatment option, and the EGPA Consensus Task Force recommendations noted that mepolizumab held promise for this condition based on the pilot studies available at the time of guideline development. IVIG can be considered for refractory EGPA or for treatment during pregnancy (Connelly-Smith et al 2023, Groh et al 2015).

Hypereosinophilic Syndrome (HES)
The World Health Organization (WHO) guidance on eosinophilic disorders has stated that identification of rearranged PDGFRA or PDGFRB is important in the management of eosinophilic disorders as those variants respond to imatinib (Shomali and Gotlib 2022). For patients with idiopathic HES (without imatinib-sensitive variants), corticosteroids are first-line therapy; second-line options include hydroxyurea, interferon-alfa, other cytotoxic chemotherapy agents, and hematopoietic stem cell transplantation. The WHO states that mepolizumab is FDA-approved for idiopathic HES, but other biologic agents are considered investigational. At the time the guidance was published, mepolizumab was FDA-approved for idiopathic HES, while other biologic agents were considered investigational.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Fasenra is an interleukin-5 receptor alpha-directed cytolytic monoclonal antibody (IgG1, kappa) indicated for:
- Add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma, and with an eosinophilic phenotype.
- Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
- Treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) without an identifiable non-hematologic secondary cause.

Limitations of Use:
- Not for relief of acute bronchospasm or status asthmaticus.

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Policy History/Revision Information

Date	Summary of Changes
11/16/2023	Approved by OptumRx P&T Committee
05/16/2024	Annual Review. New age criteria included. Updates to coverage rationale, clinical evidence, FDA and references section
05/15/2025	Annual Review. New EGPA indication included. Updates to all sections.
05/14/2026	Annual Review. Updated clinical guidelines and references.

Date	Summary of Changes
10/21/2026	Update. Added expanded indication of HES. Updated coverage rationale, billing codes, clinical evidence, guidelines, FDA, and references section.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
N/A		

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

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