Blue Cross Blue Shield Blue Care Network of Michigan

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Effective Date: 12/12/2024

Fasenra™ (benralizumab)

HCPCS: J0517

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. FDA approved indication
   c. For the diagnosis of severe eosinophilic asthma:
      i. Blood eosinophils greater than or equal to 150 cells/microliter at initiation of treatment
      ii. Chronic administration of systemic corticosteroids or high dose inhaled corticosteroids (listed in table 1) in combination with
         a) Long-acting inhaled β2 agonist (LABA) for at least 3 months fails to maintain adequate control
            OR
         b) Leukotriene modifier for at least 3 months fails to maintain adequate control
            OR
         c) Long-acting muscarininc antagonists (LAMA) in adults and children ≥ 12 years old for at least 3 months fails to maintain adequate control
      iii. Must be used as add on maintenance treatment with severe uncontrolled eosinophilic asthma
      iv. Patient is currently receiving, and will continue to receive standard of care regimen
   d. For the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA)
      i. Documentation of a consult with an allergist/immunologist or pulmonologist prior to initiation of Fasenra therapy
      ii. History or presence of asthma
      iii. At least 2 of the following criteria that are typical of EGPA
         a) Histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation
         b) Neuropathy
         c) Pulmonary infiltrates
         d) Allergic rhinitis and nasal polyps
         e) Cardiomyopathy
         f) Glomerulonephritis
         g) Alveolar hemorrhage

h) Palpable purpura
i) Antineutrophil cytoplasmic antibody (ANCA) positivity

e. The member will self-administer Fasenra unless clinically unable to do so
f. Not to be used in combination with other biologics or targeted disease-modifying antirheumatic drugs (DMARDs) for the same indication
g. Trial and failure, contraindication, OR intolerance to the preferred products as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Fasenra is the third interleukin-5 (IL-5) receptor antagonist indicated for add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype. Fasenra is also indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

- Eosinophilic asthma is a sub phenotype of severe asthma characterized by elevated sputum and blood eosinophil levels as well as increased asthma severity, atopy, late-onset disease, and steroid refractoriness.

- Severe asthma requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming uncontrolled or which remains uncontrolled despite therapy. Add-on treatment for severe asthma include LAMA, leukotriene receptor antagonist (LTRA), low dose azithromycin (adults) and biologic agents for severe allergic or severe type 2 asthma. Type 2 inflammation is found in the majority of people with severe asthma and is characterized by production of cytokines such as interleukin. Anti-IL5 monoclonal antibodies (Cinqair®, Nucala®, and Fasenra) specifically target formation of eosinophils and depletes blood eosinophil levels.

- The Global Institute for Asthma (GINA) 2023 Difficult-to-Treat & Severe Asthma Diagnosis and Management guidelines recommend those with severe asthma and Type 2 airway inflammation (blood eosinophils ≥ 150/µL and/or fractional exhaled nitric oxide (FeNO) ≥20 ppb and/or sputum eosinophils ≥2%, and/or asthma is clinically allergen driven) first should consider adherence tests and consider increasing the ICS dose for 3-6 months. Add-on Type 2-targeted biologic therapy should be considered for patients with exacerbations or poor symptom control on high dose ICS-LABA. Local payer eligibility criteria and comorbidities should also be considered. Anti-IL5/anti-IL5R, including Fasenra, is appropriate in patients with exacerbations in the last year and blood eosinophils ≥ 150/µL.

- A peripheral blood eosinophil count is an indirect way to estimate airway inflammation. A blood eosinophil count ≥ 300 cells/microliter may help to predict asthmatics who are at increased risk for exacerbations in the next year. Furthermore, a count-response relation exists between blood eosinophil counts and asthma-related outcomes. The European Respiratory Society/American Thoracic Society guidelines from 2020 suggest that treatment of severe asthma be guided by clinical criteria and biomarkers such as blood eosinophil levels or FeNO, rather than by clinical

criteria alone. In addition, it also suggests that a blood eosinophil count cut-off point of ≥ 150 cells/microliter can be used to guide anti-IL5 initiation in adult patients with severe asthma and a history of prior asthma exacerbations.

- Approval was based on results from a total of 3 multicenter, randomized, double-blind trials.
    - Two asthma exacerbation trials, SIROCCO (n = 1,204) and CALIMA (n = 1,306), randomized patients 12 to 75 years old with severe asthma not controlled on high dose (medium – high in CALIMA) ICS/LABA therapy to receive Fasenra 30 mg every 4 weeks, Fasenra 30 mg every 8 weeks, and placebo. The addition of Fasenra 30 mg SC every 8 weeks to current therapy significantly reduced asthma exacerbation rates by 51% in SIROCCO and 28% in CALIMA in patients with baseline blood eosinophil levels ≥ 300 cells/microliter.
    - The oral corticosteroid (OCS) reduction study (ZONDA) included 220 patients aged 18 years and older with severe asthma receiving high-dose ICS/LABA and chronic OCS with a baseline blood eosinophil level of ≥ 150 cells/microliter. Significantly more patients receiving Fasenra 30 mg SC every 8 weeks were able to reduce their OCS dose compared to placebo. Patients using Fasenra saw 75% reduction in median daily OCS vs. 25% in the placebo group.
- Review response to biologic therapy after 3-4 months of treatment. If the patient had a good response, the need for each medication should re-evaluated, but do not completely stop inhaled therapy. Consider gradually decreasing or stopping oral steroids first.
- Clinical reasons a patient may be unable to self-administer Fasenra include:
    - Patient or caregivers are unable to perform subcutaneous injections with proper technique
    - Member requires monthly medical support from the physician
- EGPA, formerly known as Churg-Strauss Syndrome, is a rare, immune-mediated inflammatory disease that is caused by inflammation of small to medium-sized blood vessels. It is estimated that 118,000 people throughout the world live with EGPA and approximately 15,000 patients living in the US have EGPA. EGPA can result in damage to multiple organs, including lungs, upper airway, skin, heart, gastrointestinal tract and nerves. The most common symptoms and signs include extreme fatigue, weight loss, muscle and joint pain, rashes, nerve pain, sinus and nasal symptoms, and shortness of breath. Without treatment, the disease may be fatal. Almost half (47%) of patients do not achieve remission with current treatments.
- There are limited treatment options for EGPA. Patients are often treated with chronic high-dose OCS and experience recurrent relapses when attempting to taper off OCS. Nucala is also approved for EGPA.
- Antineutrophil cytoplasmic antibodies (ANCAs) are found in 40%-60% of patients, but it is unknown whether ANCAs have a pathogenic role or if this is simply a manifestation of EGPA. EGPA is a multisystem disorder characterized by allergic rhinitis, asthma, and prominent peripheral blood eosinophilia. It primarily affects the lungs, followed by the skin, but also involves the cardiovascular, gastrointestinal, renal, and central nervous systems. Asthma is the cardinal feature of EGPA, which presents, along with allergic rhinitis and nasal polyps, long before vasculitis and the initial EGPA diagnosis. The next phase of the disease is typically eosinophilia, high levels of eosinophils in the blood, which are 5% or less in healthy patients and at least 10% and up to as high as 60% in EGPA patients. Vasculitis is the third and final phase of symptoms and includes several organs: fever, fatigue, sudden weight loss, muscle and joint pain, rash, numbness/tingling/loss of strength of hands or feet, chest pain or palpitations, shortness of breath, chronic cough, venous thrombotic events, abdominal pain, and blood in stool.
- Fasenra for EGPA was based on the MANDARA trial which was a Phase III, randomized, double-blinded, active-controlled trial that compared the efficacy and safety of Fasenra to mepolizumab in adult patients with relapsing or

refractory EGPA. In the trial, 140 patients were randomized 1:1 to receive either a single 30 mg subcutaneous injection of Fasenra or three separate 100 mg subcutaneous injections of the active comparator every four weeks.

- EGPA diagnosis was based on history or presence asthma and eosinophilia (>1.0x10^9/L and/or >10% of leucocytes) and at least 2 of the following: biopsy with eosinophilic vasculitis or perivascular/granulomatous inflammation; mono-or polyneuropathy, non-fixed pulmonary infiltrates, sino-nasal abnormality; cardiomyopathy; glomerulonephritis; alveolar haemorrhage; palpable purpura; anti neutrophil cytoplasmic anti-body (ANCA) positivity (Myeloperoxidase or proteinease 3).

- The primary endpoint was the proportion of patients who were in remission at both weeks 36 and 48. Remission is defined as Birmingham Vasculitis Activity Score (BVAS)=0 and OCS dose less than or equal to 4 mg/day. A secondary endpoint was the proportion of patients who were able to fully taper off OCS at weeks 48 through 52. The primary statistical analysis was to demonstrate non-inferiority of Fasenra versus mepolizumab based on the primary endpoint.

- In the trial, nearly 60% of Fasenra-treated patients achieved remission which was comparable to mepolizumab-treated patients. Data also showed 41% of Fasenra-treated patients fully tapered off OCS (vs. 26% in the mepolizumab arm (difference: 16%; 95% CI: 1,31)).

References:

1. Fasenra [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2024.
2. Bleecker ER, Fitzgerald JM, Chanez P, et al. Efficacy and safety of Fasenra for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomized, multicenter, placebo-controlled phase 3 trial. Lancet. 2016;388:2115-2127.
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.
4. Global Initiative for Asthma. GINA Difficult-to-treat & severe asthma in adolescent and adult patients – diagnosis and management. V4.0 August 2023. Available at: www.ginasthma.org.
5. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J 2020; 55.
6. AstraZeneca Press Release: Fasenra approved in the US for eosinophilic granulomatosis with polyangiitis https://www.astrazeneca.com/media-centre/press-releases/2024/fasenra-approved-in-the-us-for-eosinophilic-granulomatosis-with-polyangiitis.html

Table 1: Comparative cumulative daily dosing of inhaled corticosteroids (mcg/day)

Inhaled Corticosteroid	Ages 12 and up			Ages 6-11		
	Low Dose	Medium Dose	High Dose	Low Dose	Medium Dose	High Dose
Beclometasone dipropionate HFA	100 – 200	>200 – 400	>400	50 – 100	>100 – 200	>200
Budesonide DPI	200 – 400	>400 – 800	>800	100 – 200	>200 – 400	>400
Budesonide nebules	NA	NA	NA	250 – 500	>500 – 1,000	>1,000
Ciclesonide HFA	80 – 160	>160 – 320	>320	80	>80 – 160	>160
Fluticasone furoate DPI	100	NA	200	NA	NA	NA
Fluticasone propionate DPI	100 – 250	>250 – 500	>500	100 – 200	>200 – 400	>400
Fluticasone propionate HFA	100 – 250	>250 – 500	>500	100 – 200	>200 – 500	>500
Mometasone furoate	110 – 220	>220 – 440	>440	110	≥220 - <440	≥440
Triamcinolone acetonide	400 – 1,000	>1,000 – 2,000	>2,000	400 – 800	>800 – 1,200	>1,200

Policy History		
#	Date	Change Description
2.3	Effective Date: 12/12/2024	Updated to include newly approved indication for eosinophilic granulomatosis with polyangiitis.
2.2	Effective Date: 10/03/2024	Replaced the “not to be used in combination with other biologics statement for the treatment of asthma” to “not to be used in combination with other biologics or targeted DMARDs for the same indication” to align with other biologic policies
2.1	Effective Date: 10/12/2023	Annual review of policy; no changes were made to the criteria.
2.0	Effective Date: 10/06/2022	Updated to require self-administration unless clinically unable to do so
1.9	Effective Date: 10/07/2021	Updated LABA and LAMA requirement to LABA or LAMA
1.8	Effective Date: 06/10/2021	Criteria document created and criteria aligned between all biologic asthma agents. The criteria for asthma was previously part of the Biologics for Asthma Policy which will be retired
1.7	Effective Date: 08/13/2020	Criteria updated for Fasenra
1.6	Effective Date: 04/16/2020	Critieria update for step therapy to reference dosing chart for inhaled corticosteroids.
1.5	Effective Date: 12/05/2019	Updated to include Fasenra self-administered product
1.4	Effective Date: 11/07/2019	Criteria update to authorization period. Also changed languge to FDA approved age.
1.3	Effective Date: 08/15/2019	Updated criteria to account for new self-injectable Nucala formulation

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<tr><td>1.2</td><td>Effective Date: 05/09/2019</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>1.1</td><td>Effective Date: 08/07/2018</td><td>UM medical management system update for BCNA and MAPPO
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.0</td><td>Effective Date: 05/03/2018</td><td>New Drug Review
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*