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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

**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  $\beta$ 2 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 muscarinic antagonists (LAMA) in adults and children  $\geq$  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

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- 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 Initiative 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  $\geq 150/\mu\text{L}$  and/or fractional exhaled nitric oxide (FeNO)  $\geq 20$  ppb and/or sputum eosinophils  $\geq 2\%$ , 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  $\geq 150/\mu\text{L}$ .
- A peripheral blood eosinophil count is an indirect way to estimate airway inflammation. A blood eosinophil count  $\geq 300$  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  $\geq 150$  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  $\geq 300$  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  $\geq 150$  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 (ANCA) are found in 40%-60% of patients, but it is unknown whether ANCA 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 ( $>1.0 \times 10^9/L$  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 proteinase 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  $\beta_2$ -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  $\alpha$  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](http://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 nebulers	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	Criteria 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 language 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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1.2	Effective Date: 05/09/2019	Annual Review of Medical Policy										
1.1	Effective Date: 08/07/2018	UM medical management system update for BCNA and MAPPO <table border="1" data-bbox="496 268 1377 478"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
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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>.

**Blue Cross Blue Shield/Blue Care Network of Michigan**  
**Medication Authorization Request Form**  
**Fasenra™ (benralizumab) HCPCS CODE: J0517**



This form is to be used by participating physicians to obtain coverage for Fasenra™. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
<b>Name</b>	<b>Name</b>
<b>ID Number</b>	<b>Specialty</b>
<b>D.O.B.</b> <input type="checkbox"/> Male <input type="checkbox"/> Female	<b>Address</b>
<b>Diagnosis</b>	<b>City /State/Zip</b>
<b>Drug Name</b>	<b>Phone/Fax: P: (     ) -                      F: (     ) -</b>
<b>Dose and Quantity</b>	<b>NPI</b>
<b>Directions</b>	<b>Contact Person</b>
<b>Date of Service(s)</b>	<b>Contact Person Phone / Ext.</b>

**STEP 1: DISEASE STATE INFORMATION**

1. Is this request for:  Initiation  Continuation **Date patient started therapy:** \_\_\_\_\_
2. How is this medication being administered?  Self-administered **(Please fax this completed form to BCBSM at (866) 601-4425)**  
 Health Care Professional administered **(Continue to #3)**
3. Please provide reason(s) why the patient needs to have Fasenra administered by a healthcare professional:  
 Patient has co-morbidities or chronic medical conditions (such as: rheumatoid arthritis, Parkinson's disease)  
 Other: \_\_\_\_\_
4. Site of administration?  Provider office/Home infusion  Other: \_\_\_\_\_  
 Hospital outpatient facility (go to #4) **Reason for Hospital Outpatient administration:** \_\_\_\_\_
5. **Please specify location of administration if hospital outpatient infusion:** \_\_\_\_\_
6. **Please provide the NPI number for the place of administration:** \_\_\_\_\_
7. **Initiation AND Continuation of therapy:**
  - a. Please check the patient's diagnosis:  Severe eosinophilic asthma  Other: \_\_\_\_\_
  - b. What is the patient's blood eosinophil level at the initiation of therapy, in cells/microliter? \_\_\_\_\_ cells/microliter Date: \_\_\_\_\_
  - c. Which treatment(s) did not adequately control the patient's severe eosinophilic asthma symptoms after a trial of at least 3 months?  
 Systemic corticosteroid: \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 High dose inhaled corticosteroids: \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 Long acting beta2-agonist: \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 Leukotriene receptor antagonist: \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 Combination asthma inhaler with a HIGH dose corticosteroid and a long acting inhaled beta agonist: \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 Combination asthma inhaler with a MEDIUM dose corticosteroid and a long acting inhaled beta agonist: \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 Long acting muscarinic antagonist (LAMA): \_\_\_\_\_ Date: Start: \_\_\_\_\_ End: \_\_\_\_\_  
 Other: \_\_\_\_\_
  - d. Is the patient currently receiving and will continue to receive a standard of care regimen for their diagnosis with Fasenra?  
 Yes  No Comment: \_\_\_\_\_
  - e. Will the patient be using Fasenra in combination with other biologic medications for asthma (for example: Xolair, Nucala, Cinqair, or Duxipent)?  
 Yes  No Comment: \_\_\_\_\_
8. **Continuation request:** (please answer above questions as well): **Fasenra start date:** \_\_\_\_\_
  - a. Have the patient's signs and symptoms improved with Fasenra?  
 Yes  No, Comment: \_\_\_\_\_  Other: \_\_\_\_\_

Please add any other supporting medical information necessary for our review

**Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.**

Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
<b>Step 2:</b> Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Attach Chart Notes	<input type="checkbox"/> Attach Diagnostic Tests
<b>Step 3:</b> Submit	<b>By Fax: BCBSM Specialty Pharmacy Mailbox</b> <b>1-877-325-5979</b>	<b>By Mail: BCBSM Specialty Pharmacy Program</b> <b>P.O. Box 312320, Detroit, MI 48231-2320</b>

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