LOUISIANA BLUE

benralizumab (Fasenra™)

Policy # 00606
Original Effective Date: 02/21/2018
Current Effective Date: 04/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider benralizumab (Fasenra™)‡ for add-on maintenance treatment of severe asthma (eosinophilic phenotype) OR for the treatment of patients with eosinophilic granulomatosis with polyangiitis (EGPA) to be **eligible for coverage.****

Asthma

Patient Selection Criteria

Coverage eligibility for benralizumab (Fasenra) will be considered for add-on maintenance treatment of severe asthma (eosinophilic phenotype) when the following criteria are met:

Initial Authorization:

I. Fasenra is being used for the treatment of severe asthma (eosinophilic phenotype); AND
II. Patient is greater than or equal to 6 years of age; AND
III. Fasenra is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g., reslizumab (Cinqair®), omalizumab (Xolair®), mepolizumab (Nucala®), dupilumab (Dupixent®)]‡; AND
IV. Fasenra is dosed at 30 mg every 4 weeks for the first 3 doses, followed by once every 8 weeks thereafter; AND
V. Patient meets ONE of the following (a or b):
    a) Patient has a peripheral blood eosinophil count of greater than or equal to 150 cells per microliter within the past 6 weeks or within 6 weeks prior to treatment with any interleukin asthma therapy [benralizumab (Fasenra), mepolizumab (Nucala), reslizumab (Cinqair), dupilumab (Dupixent)]; OR
    b) Patient is dependent on systemic corticosteroids; AND

VI. Patient has received at least 3 consecutive months of combination therapy with BOTH of the following (a and b):
*(Note that the 3 month timeframe is an additional company requirement and will be denied as not medically necessary** if not met)*;
   a) An inhaled corticosteroid (ICS) [e.g. fluticasone products (Arnuity™ Ellipta®, Armonair™ Respiclick®)‡, mometasone products (Asmanex® Twisthaler®, Asmanex® HFA)‡, flunisolide products (Aersopan™)‡, ciclesonide products (Alvesco®)‡, budesonide products (Pulmicort Flexhaler®)‡, beclomethasone products (QVAR®)‡]; AND
   b) At least ONE of the following (1, 2, 3, or 4):
      1) Inhaled long-acting beta-agonist (LABA) [e.g., salmeterol products (Serevent® Diskus)‡, olodaterol products (Striverdi® Respimat®), indacaterol products (Arcapta™ Neohaler™)]; OR
      NOTE: Use of a combination inhaler containing both an ICS and a LABA would fulfil the requirement for both criteria a.) and b.) [e.g. fluticasone propionate and salmeterol inhalation powder/aerosol (Advair® Diskus/HFA, fluticasone/salmeterol generics, Wixela™ Inhub, AirDuo™ Respiclick)‡, budesonide and formoterol fumarate inhalation aerosol (Symbicort®)‡, fluticasone furoate and vilanterol inhalation powder (Breo® Ellipta®)‡, mometasone furoate and formoterol fumarate inhalation aerosol (Dulera®)‡].
      2) Inhaled long-acting muscarinic antagonist (LAMA) [e.g. tiotropium bromide inhalation spray (Spiriva® Respimat®, Stiolto® Respimat)‡, aclidinium products (Tudorza® Pressair®)‡, glycopyrrolate products (Seebri™ Neohaler, Bevespi™ Aerosphere, Utibron™ Neohaler), umeclidinium products (Incruse® Ellipta, Anoro® Ellipta)]; OR
      3) Leukotriene receptor antagonist (LTRA) [e.g. montelukast tablets/granules (Singulair®, generics), zafirlukast tablets (Accolate®)]‡; OR
      4) Theophylline (Theo-24, Uniphyl, TheoChron ER, generics); AND

VII. Patient's asthma continues to be uncontrolled as defined by ONE of the following (a, b, c, d, or e):
   a) Patient experienced two or more asthma exacerbations requiring treatment with systemic corticosteroids in the previous year; OR
   b) Patient experienced one or more asthma exacerbation requiring hospitalization or an Emergency Department (ED) visit in the previous year; OR
   c) Patient has a forced expiratory volume in 1 second (FEV_1) < 80% predicted; OR
   d) Patient has an FEV_1/forced vital capacity (FVC) < 0.80; OR
   e) Patient's asthma worsens upon tapering of oral corticosteroid therapy.

benralizumab (Fasenra™)

Policy # 00606
Original Effective Date: 02/21/2018
Current Effective Date: 04/01/2025

Re-Authorization
Coverage continuation for benralizumab (Fasenra) will be considered for add-on maintenance treatment of severe asthma (eosinophilic phenotype) when the following criteria are met:

I. Patient received an initial authorization for the requested drug on the same requested benefit; AND
II. Fasenra is being used for the treatment of severe asthma (eosinophilic phenotype); AND
III. Fasenra is NOT being used in combination with other monoclonal antibodies typically used to treat asthma [e.g., reslizumab (Cinqair), omalizumab (Xolair), mepolizumab (Nucala), dupilumab (Dupixent)]; AND
IV. Fasenra is dosed at 30 mg every 8 weeks; AND
V. Patient continues to receive the medications required in criterion VI. in the "Initial Criteria"; AND
VI. Patient has responded to Fasenra therapy as determined by the prescribing physician [e.g., decreased asthma exacerbations; decreased asthma symptoms; decreased hospitalizations, emergency department (ED)/urgent care, or physician visits due to asthma; decreased requirement for oral corticosteroid therapy.]
*(Note that this specific patient selection criterion is an additional company requirement and will be denied as not medically necessary** if not met)*

<u>Eosinophilic Granulomatosis with Polyangiitis</u>
<u>Patient Selection Criteria</u>
Coverage eligibility for benralizumab (Fasenra) will be considered for the treatment of EGPA when the following criteria are met:

Initial Authorization
I. Patient has a diagnosis of EGPA; AND
II. Patient is 18 years of age or older; AND
III. Patient has tried and failed (e.g., intolerance or inadequate response) a corticosteroid (e.g., prednisone) for a minimum of 4 weeks unless there is clinical evidence or patient history that suggests the use of a corticosteroid for at least 4 weeks will be ineffective or cause an adverse reaction to the patient; AND
*(Note that this specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
IV. Patient has/had a blood eosinophil level of ≥ 150 cells per microliter within the previous 6 weeks or within 6 weeks prior to treatment with any anti-interleukin therapy [e.g., reslizumab (Cinqair), omalizumab (Xolair), mepolizumab (Nucala), dupilumab (Dupixent)]; AND
V. Fasenra is dosed at 30 mg every 4 weeks.

Re-Authorization
Coverage continuation for benralizumab (Nucala) will be considered for the treatment of EGPA when the following criteria are met:

I. Patient received an initial authorization for the requested drug on the same requested benefit; AND
II. Patient has a diagnosis of EGPA; AND
III. Fasenra is dosed at 30 mg every 4 weeks; AND
IV. Patient has responded to Fasenra therapy as determined by the prescribing physician (e.g., reduced rate of relapse, corticosteroid dose reduction, reduced eosinophil levels).
*(Note that this specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of benralizumab (Fasenra) when the patient has NOT been on the pre-requisite medications for at least 3 consecutive months to be **not medically necessary.****

Based on review of available data, the Company considers the use of benralizumab (Fasenra) for EGPA when the patient has NOT tried and failed a corticosteroid for a minimum of 4 weeks to be **not medically necessary.****

Based on review on available data, the Company considers the continued use of benralizumab (Fasenra) when the patient has NOT responded to benralizumab (Fasenra) therapy as determined by the prescribing physician to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of benralizumab (Fasenra) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

Based on review of available data, the Company considers the use of benralizumab (Fasenra) for indications other than the add-on maintenance treatment of severe asthma (eosinophilic phenotype) OR the treatment of EGPA to be **investigational.***

benralizumab (Fasenra™)

Policy # 00606
Original Effective Date: 02/21/2018
Current Effective Date: 04/01/2025

Background/Overview

Fasenra is an IL-5 antagonist monoclonal antibody (IgG1 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 6 years and older, with an eosinophilic phenotype and for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA). IL-5 is expressed on the surface of eosinophils and basophils. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Fasenra binds to IL-5, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex. Inflammation is an important component in the pathogenesis of asthma and EGPA. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation. Fasenra, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of action in asthma has not been definitively established. Fasenra is provided in 30 mg/mL single dose prefilled syringes as well as 30 mg/mL single dose auto-injectors. Fasenra pre-filled syringes should be administered by a healthcare professional, while the auto-injectors are intended for administration by patients/caregivers. The dosing of Fasenra is 30 mg every 4 weeks for the first three doses, followed by once every 8 weeks thereafter for asthma and 30 mg every for weeks for EGPA.

Asthma

Asthma is a respiratory disorder characterized by increased responsiveness of the trachea and bronchi to various stimuli resulting in the narrowing of the airways, along with mucous secretion. Symptoms vary in severity and intensity and include wheezing, cough and dyspnea. Attacks can be triggered by exercise, allergens, irritants and viral infections. Based on symptoms, the four levels of asthma severity are:

- Mild intermittent (comes and goes)—you have episodes of asthma symptoms twice a week or less, and you are bothered by symptoms at night twice a month or less; between episodes, however, you have no symptoms and your lung function is normal.
- Mild persistent asthma—you have asthma symptoms more than twice a week, but no more than once in a single day. You are bothered by symptoms at night more than twice a month. You may have asthma attacks that affect your activity.
- Moderate persistent asthma—you have asthma symptoms every day, and you are bothered by nighttime symptoms more than once a week. Asthma attacks may affect your activity.
- Severe persistent asthma—you have symptoms throughout the day on most days, and you are bothered by nighttime symptoms often. In severe asthma, your physical activity is likely to be limited.

Treatment of asthma is based on a step up and step down approach based on the asthma severity and symptoms. Medications include short acting beta agonists for fast relief. Long term treatment centers around the use of inhaled corticosteroids and possible addition of medications such as long acting beta agonists, leukotriene receptor antagonists, inhaled long acting muscarinic antagonists, or theophylline.

Eosinophilic Granulomatosis with Polyangiitis
EGPA is a rare, idiopathic vasculitis that affects small to medium sized vessels. The prevalence of this condition is estimated to be around 11 to 14 cases per million persons. There are three phases of EGPA: allergic phase, eosinophilic phase, and a vasculitic phase. The allergic phase includes the development of asthma, allergic rhinitis, and sinusitis. During the eosinophilic phase, there is an increase in the eosinophil count and eosinophilic infiltration (typically in the lungs heart, and gastrointestinal system). During the vasculitis phase, patients experience necrotizing vasculitis as well as extravascular granulomatosis and symptoms including fever, malaise, and weight loss. Cardiac sequelae are the main cause of death in these patients as one of the most detrimental manifestations of EGPA are cardiac related (myocardial infarction, pericarditis, or congestive heart failure). Corticosteroids are the primary treatment of EGPA with most patients requiring continuous therapy (although still experiencing relapse). Other medications used include cyclophosphamide, azathioprine, methotrexate, etc, however no large randomized trials have been performed to effectively guide therapy beyond the use of corticosteroids. Current guidelines do not address Fasenra for EGPA.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Fasenra was approved in late 2017 for add-on maintenance treatment of patients with severe asthma aged 12 years and older, with an eosinophilic phenotype. In April 2024, Fasenra's approval expanded to include pediatric patients 6 years of age and older. In September of 2024, Fasenra was approved for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Asthma
Fasenra had three confirmatory trials and one 12 week lung function trial. Trials 1 and 2 were randomized, double-blind, parallel-group, placebo controlled exacerbation trials in patients 12 years of age and older for 48 and 56 weeks, respectively. Patients were required to be on asthma medications (inhaled corticosteroids, long acting beta agonists, oral corticosteroids, etc.) and were also stratified as having a baseline eosinophil count of greater than or equal to 300 cells/microliter OR less than 300 cells per microliter. Fasenra was given per the package insert labeled dosing. The primary endpoint for these trials was the rate of asthma exacerbations in patients with baseline blood eosinophil counts of greater than or equal to 300 cells per microliter who were taking high dose inhaled corticosteroids and long acting beta agonists. In trial 1, 35% of patients receiving Fasenra

experienced an asthma exacerbation compared to 51% on placebo. In trial 2, 40% of patients receiving Fasenra experienced an asthma exacerbation compared to 51% on placebo. In a subgroup analysis, reductions in exacerbation rates for those with baseline eosinophil counts greater than or equal to 300 cells/microliter showed a numerically greater response that those with a baseline count of less than 300 cells/microliter.

In a pooled analysis of the two confirmatory asthma exacerbation studies, patients with baseline eosinophil levels ≥ 150 cells/microliter experienced 37% reduction in the annual asthma exacerbation rate with Fasenra (at the recommended dose) compared with placebo.

Trial 3 was a randomized, double-blind, parallel-group, oral corticosteroid reduction trial. Patients were required to have daily treatment with oral corticosteroids in addition to asthma inhalers. There was an 8 week run-in period during which the oral corticosteroid was titrated to the minimum effective dose without losing asthma control. Patients were required to have eosinophils greater than or equal to 150 cells/microliter and a history of at least one exacerbation. Fasenra was given as per the package insert dosing. The primary endpoint was the percent reduction from baseline of the final oral corticosteroid dose during weeks 24 to 28, while maintaining asthma control. Compared to placebo, patients receiving Fasenra achieved greater reductions in daily maintenance oral corticosteroid dose while maintaining asthma control. The median percent reduction in daily OCS dose from baseline was 75% in those receiving Fasenra compared to 25% in patients receiving placebo. Reductions of 50% or higher in oral corticosteroid dose were observed in 66% of those receiving Fasenra compared to 37% receiving placebo. The proportion of patients with a mean final dose less than or equal to 5 mg at weeks 24 to 28 was 59% for Fasenra and 33% for placebo. Only patients with an optimized baseline oral corticosteroid dose of 12.5 mg or less were eligible to achieve a 100% reduction in oral corticosteroid dose during the study. Of those patients, 52% receiving Fasenra and 19% on placebo achieved a 100% reduction in the oral corticosteroid dose.

Change from baseline in mean FEV_1 was assessed in these 3 trials as a secondary endpoint. Compared with placebo, Fasenra provided consistent improvements over time in the mean change from baseline in FEV_1.

Eosinophilic Granulomatosis with Polyangiitis
Fasenra was studied in one randomized, double-blind, active-controlled, noninferiority clinical trial that enrolled 140 adults with EGPA. Patients were required to have asthma, eosinophilia (1,000 cells/uL or > 10% of leukocytes) and a history of relapsing or refractory disease treated with background prednisolone/prednisone with or without immunosuppressive therapy. Patients were randomized to receive Fasenra 30 mg administered subcutaneously every 4 weeks or mepolizumab 300 mg administered subcutaneously every 4 weeks in addition to continued background therapy. Starting at week 4, the oral corticosteroid (OCS) dose was tapered at the discretion of the investigator. The primary endpoint in the trial was the proportion of patients in remission, defined

as Birmingham Vasculitis Activity Score (BVAS) = 0 (no active vasculitis) plus prednisolone/prednisone dose ≤ 4 mg/day, at both week 36 and week 48. Fasenra demonstrated noninferiority to mepolizumab for the primary endpoint of remission and the components of remission.

References

1. Fasenra [package insert]. AstraZeneca. Wilmington, Delaware. Updated September 2024.
2. Fasenra Prior Authorization Policy. Express Scripts. December 2018.
3. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3). National Heart, Lung, and Blood Institute. www.nhlbi.nih.gov/guidelines/asthma.
4. FitzGerald JM, Bleecker ER, Menzies-Gow A, et al. Predictors of enhanced response with benralizumab for patients with severe asthma: pooled analysis of the SIROCCO and CALIMA studies. Lancet Respir Med. 2018;6(1):51-64.

Policy History

Original Effective Date: 02/21/2018
Current Effective Date: 04/01/2025

02/01/2018	Medical Policy Committee review
02/21/2018	Medical Policy Implementation Committee approval. New policy.
02/07/2019	Medical Policy Committee review
02/20/2019	Medical Policy Implementation Committee approval. Changed eosinophil count from 300 cells/microliter to 150 cells/microliter.
02/06/2020	Medical Policy Committee review
02/12/2020	Medical Policy Implementation Committee approval. Added information about the self-injectable dosage form. Updated inhalers within criteria.
02/04/2021	Medical Policy Committee review
02/10/2021	Medical Policy Implementation Committee approval. Clarified that for a continuation request, an initial authorization must be present on the same benefit. No coverage changes.
02/03/2022	Medical Policy Committee review
02/09/2022	Medical Policy Implementation Committee approval. Criteria eligibility unchanged.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Criteria eligibility unchanged.
02/01/2024	Medical Policy Committee review
02/14/2024	Medical Policy Implementation Committee approval. Criteria eligibility unchanged.

benralizumab (Fasenra™)

Policy # 00606
Original Effective Date: 02/21/2018
Current Effective Date: 04/01/2025

05/02/2024	Medical Policy Committee review
05/08/2024	Medical Policy Implementation Committee approval. Updated criteria to reflect FDA approval in pediatric patients 6 years of age and older. Also updated criteria to require patients to be corticosteroid dependent if the eosinophil count is not >=150 cells/μL. Removed mention of Flovent from policy.
03/06/2025	Medical Policy Committee review
03/12/2025	Medical Policy Implementation Committee approval. Added new indication, EGPA, to the policy with criteria. Updated relevant sections.

Next Scheduled Review Date: 03/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0517
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

benralizumab (Fasenra™)

Policy # 00606
Original Effective Date: 02/21/2018
Current Effective Date: 04/01/2025

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.