

# Highmark Commercial Medical Policy-PA/WV/DE/NY

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<b>Medical Policy:</b>	I-146-0234
<b>Topic (or Title):</b>	Monoclonal Antibodies for the Treatment of Asthma and Eosinophilic Conditions
<b>Section:</b>	Injections
<b>Effective Date:</b>	February 2, 2026 July 20, 2026
<b>Issued Date:</b>	February 2, 2026 July 20, 2026
<b>Last Revision Date:</b>	January 2026 May 2026
<b>Annual Review:</b>	May 2026

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Benralizumab (Fasenra™) is an interleukin-5 receptor alpha-directed cytolytic monoclonal antibody (IgG1, kappa) indicated for add-on maintenance treatment of individuals with severe asthma aged 12 years and older, and with an eosinophilic phenotype or as add-on maintenance treatment for eosinophilic granulomatosis with polyangiitis (EPGA).

Mepolizumab (Nucala®) is a humanized monoclonal antibody against interleukin-5 (IL-5). IL-5 is the predominant cytokine responsible for the growth and differentiation, recruitment, activation and survival of eosinophils. Mepolizumab binds to IL-5 with a dissociation constant of 100 pM, inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. Inhibition of IL-5 signaling reduces the production and survival of eosinophils.

Reslizumab (Cinqair®) is an interleukin-5 antagonist monoclonal antibody (IgG4 kappa) indicated for add-on maintenance treatment of individuals with severe asthma aged 18 years and older, and with an eosinophilic phenotype.

Tezepelumab-ekko (Tezspire™) is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody (IgG2λ), indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma or chronic rhinosinusitis with nasal polyps (CRSwNP).

Depemokimab-ulaa (Exdensur™) is an interleukin-5 antagonist monoclonal antibody (IgG1 kappa) indicated for add-on maintenance treatment of individuals with severe asthma aged 12 years and older, and with an eosinophilic phenotype.

## Policy Position

### Preferred Products

Benralizumab (Fasenra) and mepolizumab (Nucala) are the preferred interleukin-5 antagonist products for all individuals for asthma indications. The initial authorization will be valid for up to 12 months and the reauthorization will be valid for up to 12 months.

Preferred product requirements are only applicable to interleukin-5 antagonists and do not apply to other treatment options for severe asthma (i.e. thymic stromal lymphopoietin (TSLP) blockers, IL-4/IL-13 antagonists, IgE antibodies).

### Procedure Codes

J0517

J2182

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### Non-Preferred Injectable Product

In order for a request for a non-preferred interleukin-5 antagonist product [reslizumab (Cinqair), depemokimab-ulaa (Exdensur)] to be approved the individual must have had an adequate therapeutic

trial and experienced a documented drug therapy failure or intolerance to both of the preferred products. The initial authorization will be valid for up to 12 months and the reauthorization will be valid for up to 12 months.

Adequate therapeutic trial is defined as four (4) months from first dose of therapy at Food and Drug Administration (FDA) or compendia based therapeutic doses of preferred product.

### Procedure Codes

J2786

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Benralizumab (Fasenra) may be considered medically necessary when the following criteria are met:

#### Severe Asthma

- Individual is six (6) years of age or older; **and**
- Individual diagnosed with severe asthma with an eosinophilic phenotype; **and**
- Benralizumab (Fasenra) will be used as an add-on maintenance treatment; **and**
- Individual is currently being treated with medium or high dose ICS plus at least three (3) months of treatment with a long-acting beta agonist (LABA) and additional asthma controller medications (LAMA, LTRA), unless the individual is intolerant of, or has a medical contraindication to all of these agents; **and**
- Asthma is classified as uncontrolled or inadequately controlled as defined as **ONE** of the following:
  - Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT consistently less than 20); **or**
  - A history of two (2) or more exacerbations in the last 12 months requiring oral or systemic corticosteroid treatment; **or**
  - A documented reduced lung function [pre-bronchodilator forced expiratory volume (FEV<sub>1</sub>) below 80% in adults, and below 90% in adolescents]; **and**
- The individual has **ONE** of the following blood eosinophil count (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection):
  - Greater than or equal to 150 cells/microliter within six (6) weeks of initiation of therapy; **or**
  - Greater than or equal to 300 cells/microliter within twelve (12) months of initiation of therapy; **and**
- Individual is not receiving benralizumab (Fasenra) in combination with mepolizumab (Nucala), omalizumab (Xolair), **an omalizumab biosimilar**, reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months.

#### Reauthorization Criteria for Asthma

Continuation of therapy with benralizumab (Fasenra) may be considered medically necessary for the treatment of an individual with documented severe eosinophilic asthma when the following criteria are met:

- Treatment with benralizumab (Fasenra) has resulted in clinical improvement as documented by **ONE** or more of the following:
  - Decreased utilization of rescue medications; **or**
  - Decreased frequency of exacerbations; **or**
  - Increase in predicted forced expiratory volume in one second (FEV<sub>1</sub>) from pretreatment baseline; **or**
  - Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing; **and**

- Individual is not receiving benralizumab (Fasenra) in combination with mepolizumab (Nucala), omalizumab (Xolair), **an omalizumab biosimilar**, reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Reauthorization will be for up to 12 months.

### Eosinophilic Granulomatosis with Polyangiitis (EGPA)

- Individual 18 years of age or older; **and**
- Individual diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA); **and**
- Documented history of relapsing or refractory disease; **and**
- Individual is on a stable dosage of oral prednisolone or prednisone for four (4) weeks; **and**
- Individual will be receiving standard of care while on therapy (glucocorticoid treatment (prednisone or prednisolone), with or without immunosuppressive therapy (cyclosporine, leflunomide, azathioprine etc.); **and**
- Initial authorization will be for up to 12 months.

### Reauthorization Criteria for EGPA

Continuation of therapy with benralizumab (Fasenra) after twelve (12) months may be considered medically necessary for the treatment of an individual with documented EGPA when the following criteria are met:

- Treatment with benralizumab (Fasenra) resulted in an improvement of individuals condition; **and**
- Reauthorization will be for up to 12 months.

The use of benralizumab (Fasenra) not meeting the criteria as indicated in this policy is considered not medically necessary.

### Procedure Codes

J0517

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Mepolizumab (Nucala) may be considered medically necessary for use in individuals who meet the following criteria for any **ONE** (1) of the indications listed below:

### Severe Asthma

- Individual aged six (6) years or older; **and**
- Individual diagnosed with severe asthma with an eosinophilic phenotype; **and**
- Mepolizumab (Nucala) will be used as an add-on maintenance treatment; **and**
- Individual is currently being treated with high dose ICS plus at least three (3) months of treatment with a controller medication (either a LABA, LTRA, or theophylline), unless the individual is intolerant of, or has a medical contraindication to all of these agents; **and**
- Asthma is classified as uncontrolled or inadequately controlled as defined as **ONE** of the following:
  - Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT consistently less than 20); **or**
  - A history of two (2) or more exacerbations requiring oral or systemic corticosteroid treatment; **or**
  - A documented reduced lung function [pre-bronchodilator forced expiratory volume (FEV<sub>1</sub>) below 80% in adults, and below 90% in adolescents]; **and**

- The individual has **ONE** of the following blood eosinophil counts (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection):
  - Greater than or equal to 150 cells/microliter within six (6) weeks of initiation of therapy; **or**
  - Greater than or equal to 300 cells/microliter within twelve (12) months of initiation of therapy; **and**
- Individual is not receiving mepolizumab (Nucala) in combination with benralizumab (Fasenra), omalizumab (Xolair), [an omalizumab biosimilar](#), reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months.

### Reauthorization Criteria for Asthma

Continuation of therapy with mepolizumab (Nucala) may be considered medically necessary for the treatment of an individual with documented severe eosinophilic asthma when the following criteria are met:

- Treatment with mepolizumab (Nucala) has resulted in clinical improvement as documented by **ONE** or more of the following:
  - Decreased utilization of rescue medications; **or**
  - Decreased frequency of exacerbations; **or**
  - Increase in predicted forced expiratory volume in one second (FEV1) from pretreatment baseline; **or**
  - Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing; **and**
- Individual is not receiving mepolizumab (Nucala) in combination with benralizumab (Fasenra), omalizumab (Xolair), [an omalizumab biosimilar](#), reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Reauthorization will be for up to 12 months.

### Eosinophilic Granulomatosis with Polyangiitis (EGPA)

- Individual 18 years of age or older; **and**
- Individual diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA); **and**
- Documented history of relapsing or refractory disease; **and**
- Individual is on a stable dosage of oral prednisolone or prednisone for four (4) weeks; **and**
- Individual will be receiving standard of care while on therapy (glucocorticoid treatment (prednisone or prednisolone), with or without immunosuppressive therapy (cyclosporine, leflunomide, azathioprine etc.); **and**
- Initial authorization will be for up to 12 months..

### Reauthorization Criteria for EGPA

Continuation of therapy with mepolizumab (Nucala) after twelve (12) months may be considered medically necessary for the treatment of an individual with documented EGPA when the following criteria are met:

- Treatment with mepolizumab (Nucala) resulted in an improvement of individual's condition; **and**
- Reauthorization will be for up to 12 months.

### Hypereosinophilic Syndrome (HES)

- Individual 12 years of age or older; **and**

- Individual diagnosed with HES for greater than or equal to six (6) months; **and**
- There is no identifiable non-hematologic secondary cause of HES (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy); **and**
- Individual does not have FIP1L1-PDGFR $\alpha$  kinase-positive HES; **and**
- Individual has experienced at least two (2) HES flares (defined as HES-related worsening of clinical symptoms or blood eosinophil counts requiring an escalation in therapy) within the past 12 months; **and**
- Individual has a blood eosinophil count of 1,000 cells/mcL or higher prior to starting mepolizumab (Nucala); **and**
- Individual is on stable HES therapy (chronic or episodic oral corticosteroids, immunosuppressive, or cytotoxic therapy) for at least four (4) weeks prior to initiation of mepolizumab (Nucala); **and**
- Initial authorization will be for up to 12 months.

### Reauthorization Criteria for HES

Continuation of therapy with mepolizumab (Nucala) may be considered medically necessary for the treatment of an individual with documented HES when the following criteria are met:

- Treatment with mepolizumab (Nucala) resulted in a decrease in HES flares; **and**
- Reauthorization will be for up to 12 months.

### Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

- Individual is 18 years or older; **and**
- Individual is diagnosed with CRSwNP **and**
- Mepolizumab (Nucala) will be used as an add-on maintenance treatment; **and**
- Individual experienced inadequate results to nasal corticosteroids for at least eight (8) weeks of use unless not tolerated or contraindicated; **and**
- Diagnosis confirmed by **ANY TWO** (2) of the following symptoms:
  - Nasal drainage; **or**
  - Nasal blockage/obstruction/congestion; **or**
  - Facial pressure or pain; **or**
  - Decrease or loss in sense of smell lasting for at least 12 weeks; **and**
- Individual has bilateral polyps diagnosed by nasal endoscopy or CT scan; **and**
- Individual has bilateral Nasal Polyp Score (NPS) greater than or equal to 5 with greater than or equal to 2 in each nostril; **and**
- Individual has Visual analog scale (VAS) score of greater than 5; **and**
- Individual had at least one surgery in the previous 10 years for removal of nasal polyps; **and**
- Individual is not receiving mepolizumab (Nucala) in combination with benralizumab (Fasenra), omalizumab (Xolair) reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months.

### Reauthorization Criteria for CRSwNP

Continuation of therapy with mepolizumab (Nucala) may be considered medically necessary for the treatment of an individual with documented CRSwNP when the following criteria are met:

- Individual is not receiving mepolizumab (Nucala) in combination with benralizumab (Fasenra), omalizumab (Xolair) reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Treatment with mepolizumab (Nucala) resulted in improvement in signs and symptoms of CRSwNP documented by improvement in VAS score; **and**

- Reauthorization will be for up to 12 months.

### Chronic Obstructive Pulmonary Disease (COPD)

- Individual is 18 years or older; **and**
- Individual is diagnosed with COPD **and**
- Individual has a post-bronchodilator FEV<sub>1</sub> less than or equal to 80% predicted; **and**
- The individual has **ONE (1)** or more of the following:
  - A blood eosinophilic count of greater than or equal to 300 cells/mcL; **or**
  - Individual is currently taking daily or alternate-day oral corticosteroids; **and**
- Individual has a modified Medical Research Council dyspnea scale score of greater than or equal to 2; **and**
- Individual meets ONE (1) or more of the following criteria:
  - An exacerbation history of at least two (2) moderate exacerbations resulting in treatment with systemic corticosteroids and/or antibiotics in the previous year; **or**
  - One (1) severe exacerbation resulting in hospitalization or observation in the emergency department for over 24 hours in the previous year; **or**
  - GOLD group E; **and**
- Individual has inadequate symptom control despite regular treatment for at least three (3) months with triple therapy consisting of a long-acting muscarinic antagonist (LAMA), long-acting beta agonist (LABA), and inhaled corticosteroid (ICS) (LAMA/LABA/ICS), unless intolerant of, or has contraindications to these agents; **and**
- Individual is not receiving mepolizumab (Nucala) in combination with benralizumab (Fasenra), omalizumab (Xolair), **an omalizumab biosimilar**, reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to up to 12 months.

### Reauthorization Criteria for COPD

Continuation of therapy with mepolizumab (Nucala) may be considered medically necessary for the treatment of an individual with documented COPD when the following criteria are met:

- Treatment with mepolizumab (Nucala) has resulted in clinical improvement as documented by **ONE** or more of the following:
  - Reduction in symptoms of COPD; **or**
  - Decreased frequency of exacerbations; **or**
  - Improvement in exercise tolerance; **or**
  - Delay in disease progression; **and**
- Individual is not receiving mepolizumab (Nucala) in combination with benralizumab (Fasenra), omalizumab (Xolair), **an omalizumab biosimilar**, reslizumab (Cinqair), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Reauthorization will be for up to up to 12 months.

The use of mepolizumab (Nucala) not meeting the criteria as indicated in this policy is considered not medically necessary.

### Procedure Codes

J2182

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Reslizumab (Cinqair) may be considered medically necessary when the following criteria are met:

- Individual is 18 years of age or older; **and**
- Individual diagnosed with severe asthma with an eosinophilic phenotype; **and**

- Reslizumab (Cinqair) will be used as an add-on maintenance treatment; **and**
- Individual is currently being treated with high-dose ICS plus at least three (3) months of an additional controller (e.g., LABA, LTRA, or theophylline) medication, unless contraindicated; **and**
- Asthma is classified as uncontrolled or inadequately controlled as defined as **ONE** of the following:
  - Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT consistently less than 20); **or**
  - A history of two (2) or more exacerbations in the last 12 months requiring oral or systemic corticosteroid treatment; **or**
  - A documented reduced lung function [pre-bronchodilator forced expiratory volume (FEV1) below 80% in adults, and below 90% in adolescents]; **and**
- Has blood eosinophils of 400 cells/ $\mu$ L or higher within four (4) weeks of initiation of therapy; **and**
- Individual is not receiving Reslizumab (Cinqair) in combination with benralizumab (Fasenra), omalizumab (Xolair), an omalizumab biosimilar, mepolizumab (Nucala), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months.

### Reauthorization Criteria

Continuation of therapy with Reslizumab (Cinqair) may be considered medically necessary for the treatment of an individual with documented severe eosinophilic asthma when the following criteria are met:

- Treatment with Reslizumab (Cinqair) has resulted in clinical improvement as documented by **ONE** or more of the following:
  - Decreased utilization of rescue medications; **or**
  - Decreased frequency of exacerbations; **or**
  - Increase in predicted FEV1 from pretreatment baseline; **or**
  - Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing; **and**
- Individual is not receiving Reslizumab (Cinqair) in combination with benralizumab (Fasenra), omalizumab (Xolair), an omalizumab biosimilar, mepolizumab (Nucala), depemokimab-ulaa (Exdensur), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Reauthorization will be for up to 12 months.

The use of reslizumab (Cinqair) not meeting the criteria as indicated in this policy is considered not medically necessary.

### Procedure Codes

J2786

Tezepelumab-ekko (Tezspire) may be considered medically necessary when **ALL** of the following criteria are met:

### Severe Asthma

- Individual is 12 years of age or older; **and**
- Individual is diagnosed with severe, uncontrolled asthma; **and**
- Individual has been receiving medium to high dose inhaled corticosteroid (ICS) for at least 3 months, unless the individual is intolerant of, or has a medical contraindication to all of these agents; **and**
- Individual has been receiving at least one (1) additional controller medication [e.g., long-acting beta agonist (LABA), long-acting muscarinic antagonists (LAMA), or leukotriene receptor antagonists (LTRA)] with or without oral corticosteroid (OCS) for at least 3 months, unless the individual is intolerant of, or has a medical contraindication to all of these agents; **and**

- Tezepelumab-ekko (Tezspire) will be used as add-on maintenance treatment; **and**
- Asthma is classified as uncontrolled or inadequately controlled as defined as **ONE** of the following:
  - Poor symptom control (e.g., ACQ-6 score consistently greater than 1.5 or ACT consistently less than 20); **or**
  - A history of two (2) or more exacerbations in the last 12 months requiring oral or systemic corticosteroid treatment; **or**
  - A documented reduced lung function [pre-bronchodilator forced expiratory volume (FEV1) below 80% in adults, and below 90% in adolescents 12-17 years old]; **and**
- Individual is not currently receiving benralizumab (Fasenra), mepolizumab (Nucala), omalizumab (Xolair), [an omalizumab biosimilar](#), reslizumab (Cinqair), depemokimab-ulaa (Exdensur) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months..

### Reauthorization Criteria for Severe Asthma

Continuation of therapy with tezepelumab-ekko (Tezspire) may be considered medically necessary for the treatment of an individual with documented severe asthma when **ALL** of the following criteria are met:

- Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing; **and**
- Treatment with tezepelumab-ekko (Tezspire) has resulted in clinical improvement as documented by **ONE** or more of the following:
  - Decreased utilization of rescue medications; **or**
  - Decreased frequency of exacerbations; **or**
  - Increase in predicted forced expiratory volume in one second (FEV1) by 10% from pretreatment baseline; **or**
  - Decrease in ACQ-6 score by 0.5 or increase in ACT by 3 from pretreatment baseline.
- Individual will continue on maintenance ICS and additional controller medication; **and**
- Individual is not currently receiving benralizumab (Fasenra), mepolizumab (Nucala), omalizumab (Xolair), [an omalizumab biosimilar](#), reslizumab (Cinqair), depemokimab-ulaa (Exdensur) or dupilumab (Dupixent); **and**
- Reauthorization will be for up to 12 months; **or**

### Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

- Individual is 12 years or older; **and**
- Individual is diagnosed with CRSwNP **and**
- Tezepelumab-ekko (Tezspire) will be used as an add-on maintenance treatment; **and**
- Individual experienced inadequate results to nasal corticosteroids for at least eight (8) weeks of use unless not tolerated or contraindicated; **and**
- Diagnosis confirmed by **ANY TWO** (2) of the following symptoms:
  - Nasal drainage; **or**
  - Nasal blockage/obstruction/congestion; **or**
  - Facial pressure or pain; **or**
  - Decrease or loss in sense of smell lasting for at least 12 weeks; **and**
- Individual has bilateral polyps diagnosed by nasal endoscopy or CT scan; **and**
- Individual has bilateral Nasal Polyp Score (NPS) greater than or equal to 5 with greater than or equal to 2 in each nostril; **and**
- Individual has Visual analog scale (VAS) score of greater than 5; **and**
- Individual had at least one surgery in the previous 10 years for removal of nasal polyps; **and**
- Individual is not receiving tezepelumab-ekko (Tezspire) in combination with benralizumab (Fasenra), omalizumab (Xolair), [an omalizumab biosimilar](#), reslizumab (Cinqair), mepolizumab (Nucala), depemokimab-ulaa (Exdensur) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months.

## Reauthorization Criteria for CRSwNP

Continuation of therapy with tezepelumab-ekko (Tezspire) may be considered medically necessary for the treatment of an individual with documented CRSwNP when the following criteria are met:

- Individual is not currently receiving benralizumab (Fasenra), mepolizumab (Nucala), omalizumab (Xolair), [an omalizumab biosimilar](#), reslizumab (Cinqair), depemokimab-ulaa (Exdensusur) or dupilumab (Dupixent); **and**
- Treatment with tezepelumab-ekko (Tezspire) resulted in improvement in signs and symptoms of CRSwNP documented by improvement in VAS score; **and**
- Reauthorization will be for up to 12 months.

The use of tezepelumab-ekko (Tezspire) not meeting the criteria as indicated in this policy is considered not medically necessary.

## Procedure Codes

J2356

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Depemokimab-ulaa (Exdensusur) may be considered medically necessary when the following criteria are met:

- Individual is 12 years of age or older; **and**
- Individual diagnosed with severe asthma with an eosinophilic phenotype; **and**
- Depemokimab-ulaa (Exdensusur) will be used as an add-on maintenance treatment; **and**
- Individual is currently being treated with high-dose ICS plus at least three (3) months of an additional controller (e.g., LABA, LTRA, or theophylline) medication, unless contraindicated; **and**
- Asthma is classified as uncontrolled or inadequately controlled as defined as **ONE** of the following:
  - Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT consistently less than 20); **or**
  - A history of two (2) or more exacerbations in the last 12 months requiring oral or systemic corticosteroid treatment; **or**
  - A documented reduced lung function [pre-bronchodilator forced expiratory volume (FEV1) below 80% in adults, and below 90% in adolescents]; **and**
- The individual has **ONE** of the following blood eosinophil count (in the absence of other potential causes of eosinophilia, including hypereosinophilic syndromes, neoplastic disease, and known or suspected parasitic infection):
  - Greater than or equal to 150 cells/microliter within six (6) weeks of initiation of therapy; **or**
  - Greater than or equal to 300 cells/microliter within twelve (12) months of initiation of therapy; **and**
- Individual is not receiving depemokimab-ulaa (Exdensusur) in combination with benralizumab (Fasenra), omalizumab (Xolair), [an omalizumab biosimilar](#), mepolizumab (Nucala), reslizumab (Cinqair), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Initial authorization will be for up to 12 months.

## Reauthorization Criteria

Continuation of therapy with depemokimab-ulaa (Exdensusur) may be considered medically necessary for the treatment of an individual with documented severe eosinophilic asthma when the following criteria are met:

- Treatment with depemokimab-ulaa (Exdensur) has resulted in clinical improvement as documented by **ONE** or more of the following:
  - Decreased utilization of rescue medications; **or**
  - Decreased frequency of exacerbations; **or**
  - Increase in predicted FEV1 from pretreatment baseline; **or**
  - Reduction in reported asthma-related symptoms, such as, asthmatic symptoms upon awakening, coughing, fatigue, shortness of breath, sleep disturbance, or wheezing; **and**
- Individual is not receiving depemokimab-ulaa (Exdensur) in combination with benralizumab (Fasenra), omalizumab (Xolair), [an omalizumab biosimilar](#), mepolizumab (Nucala), reslizumab (Cinqair), tezepelumab (Tezspire) or dupilumab (Dupixent); **and**
- Reauthorization will be for up to 12 months.

The use of depemokimab-ulaa (Exdensur) not meeting the criteria as indicated in this policy is considered not medically necessary.

### Procedure Codes

J3590

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**NOTE:** In addition to the above criteria, product specific dosage and/or frequency limits may apply in accordance with the U.S. Food and Drug Administration (FDA)-approved product prescribing information, national compendia, Centers for Medicare and Medicaid Services (CMS) and other peer reviewed resources or evidence-based guidelines. Highmark may deny, in full or in part, reimbursement for utilization that does not fall within the applicable dosage and/or frequency limits.

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### References

1. [Ortega H, Liu M, Pavord I, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. \*New Engl J Med.\* 2014; 371\(13\):1198-1207.](#)
2. [Prazma CM, Wenzel S, Barnes N, et al. Characterisation of an oral corticosteroids \(OCS\) dependent severe asthma population treated with mepolizumab. \*Thorax.\* 2014; 69\(12\):1141-1142.](#)
3. [Katz, L, Gleich G, Hartley B, et al. Blood eosinophil count is a useful biomarker to identify patients with severe eosinophilic asthma. \*Annals Am Thor Soc.\* 2014;11\(4\):531-536.](#)
4. [Chung KF, Wenzel SE, Brozek JL, et al. International European Respiratory Society/American Thoracic Society guidelines on definition, evaluation and treatment of severe asthma. \*Eur Respir J.\* 2014;43\(2\):343-373.](#)
5. [Spergel JM, Rothenberg ME, Collins MH, et al. Reslizumab in children and adolescents with eosinophilic esophagitis: Results of a double-blind, randomized, placebo-controlled trial. \*J Allergy Clin Immunol.\* 2012;456-463.](#)
6. [Bjerner L, Lerner C, Maspero J, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil levels. \*CHEST.\* 2016;150\(4\):789-798.](#)
7. [Pham T, Damera G, Newbold P, & Ranade K. Reductions in eosinophil biomarkers by benralizumab in patients with asthma. \*Respiratory Medicine.\* 2016;111:21-29.](#)

8. [Goldman M, Hirsch I, Zangrilli J G, et al. The association between blood eosinophil count and benralizumab efficacy for patients with severe, uncontrolled asthma: Subanalyses of the phase III SIROCCO and CALIMA studies. \*Curr Med Res Opin.\* 2017;33\(9\):1605-1613.](#)
9. [FitzGerald J M, Bleecker, E R, 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.\* 2018;6:51-64.](#)
10. [Wechsler M E, Akuthota P, Jayne D, et al. Mepolizumab or placebo for eosinophilic granulomatosis with polyangiitis. \*New Engl J Med.\* 2017;376\(20\):1921-1932.](#)
11. [Chung K, Wenzel S, Brozek J, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. \*Euro Resp J.\* 2014;43:343-373.](#)
12. [Roufosse F, Kahn J, Rothenberg M, et al. Efficacy and safety of mepolizumab in hypereosinophilic syndrome: a Phase III, randomized, placebo-controlled trial. \*J Aller and Clin Immuno.\* 2020.](#)
13. [Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023.](#)
14. [Corren J, Parnes J, Wang L, et al. Tezepelumab in adults with uncontrolled asthma. \*N Engl J Med.\* 2017;377\(10\):936-946.](#)
15. [Corren J, Garcia Gil E, Griffiths J, et al. Tezepelumab improves patient-reported outcomes in patients with severe, uncontrolled asthma in PATHWAY. \*Ann Allergy Asthma Immunol.\* 2021;126\(2\):187-193.](#)
16. [Menzies-Gow A, Colice G, Griffiths J, et al. NAVIGATOR: a phase 3 multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy and safety of tezepelumab in adults and adolescents with severe, uncontrolled asthma. \*Respir Res.\* 2020;21\(1\):266.](#)
17. [Menzies-Gow A, Ponnarambil S, Downie J, Bowen K, Hellqvist Å, Colice G. DESTINATION: a phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the long-term safety and tolerability of tezepelumab in adults and adolescents with severe, uncontrolled asthma. \*Respir Res.\* 2020;21\(1\):279.](#)
18. [Menzies-Gow A, Corren J, Bourdin A, et al. Tezepelumab in adults and adolescents with severe, uncontrolled asthma. \*N Engl J Med.\* 2021;384\(19\):1800-1809.](#)
19. [Han JK, Bachert C, Fokkens W, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps \(SYNAPSE\): A randomised, double-blind, placebo-controlled, phase 3 trial. \*Lancet Respir Med.\* 2021;9\(10\):1141-1153.](#)
20. [Jackson DJ, Wechsler ME, Jackson DJ, et al.; Twice-yearly depemokimab in severe asthma with an eosinophilic phenotype. \*NEJM.\* 2024 Dec 19;391\(24\):2337-2349.](#)
21. [Benralizumab In: AHFS Drug Information Online Electronic Medical Library. Bethesda, MD: American Society of Health-System Pharmacists. Updated February 10, 2025.](#)
22. [Mepolizumab In: AHFS Drug Information Online Electronic Medical Library. Bethesda, MD: American Society of Health-System Pharmacists. Updated August 28, 2023.](#)

23. [Reslizumab In: AHFS Drug Information Online Electronic Medical Library. Bethesda, MD: American Society of Health-System Pharmacists. Updated March 22, 2017.](#)
24. [Tezepelumab In: AHFS Drug Information Online Electronic Medical Library. Bethesda, MD: American Society of Health-System Pharmacists. Updated September 10, 2024.](#)
25. [Clinical Pharmacology™ Compendium. 2026. Tampa FL: Gold Standard, Inc. Benralizumab.](#)
26. [Clinical Pharmacology™ Compendium. 2026. Tampa FL: Gold Standard, Inc. Mepolizumab.](#)
27. [Clinical Pharmacology™ Compendium. 2026. Tampa FL: Gold Standard, Inc. Reslizumab.](#)
28. [Clinical Pharmacology™ Compendium. 2026. Tampa FL: Gold Standard, Inc. Tezepelumab.](#)
29. [Clinical Pharmacology™ Compendium. 2026. Tampa FL: Gold Standard, Inc. Depemokimab.](#)
30. [Micromedex DrugDex Compendium®. 2026. Benralizumab.](#)
31. [Micromedex DrugDex Compendium®. 2026. Mepolizumab.](#)
32. [Micromedex DrugDex Compendium®. 2026. Reslizumab.](#)
33. [Micromedex DrugDex Compendium®. 2026. Tezepelumab-ekko.](#)
34. [Micromedex DrugDex Compendium®. 2026. Depemokimab-ulaa.](#)
35. [Fasenra \(benralizumab\) injection, for subcutaneous use \[package insert\]. AstraZeneca Pharmaceuticals LP. Wilmington, DE. Revised 09/2024.](#)
36. [Cinqair \(Reslizumab\) injection \[package insert\]. Teva Respiratory, LLC. West Chester, PA. Revised 02/2020.](#)
37. [Nucala \(mepolizumab\) \[package insert\]. GlaxoSmithKline LLC. Philadelphia, PA. Revised 08/2025.](#)
38. [Tezspire™ \(Tezepelumab-ekko\) for injection, for subcutaneous use \[package insert\]. Amgen Inc. Thousand Oaks, CA. Revised 10/2025.](#)
39. [Exdensusur™ \(depemokimab-ulaa\) for injection, for subcutaneous use \[package insert\]. GlaxoSmithKline LLC. Philadelphia, PA. Revised 12/2025.](#)

**Diagnosis Codes  
Covered Diagnosis Codes for J0517**

J45.50      J45.51      J45.52      J82.83      J82.89      M30.1

**Covered Diagnosis Codes for J2786, J3590**

J45.50      J45.51      J45.52      J82.83      J82.89

#### Covered Diagnosis Codes for Procedure Code J2182

D72.110	D72.119	J33.0	J33.1	J33.8	J33.9	J45.50
J45.51	J45.52	J82.83	J82.89	M30.1		

#### Covered Diagnosis Codes for J2356

J33.0	J33.1	J33.8	J33.9	J45.50	J45.51
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### Place of Service: Outpatient

The administration of Benralizumab (Fasenra), Mepolizumab (Nucala), Reslizumab (Cinqair), depemokimab-ulaa (Exdensur)\_ or tezepelumab-ekko (Tezspire) is typically an outpatient procedure which is only eligible for coverage as an inpatient procedure in special circumstances, including, but not limited to, the presence of a co-morbid condition that would require monitoring in a more controlled environment such as the inpatient setting.

### The policy position applies to all commercial lines of business

*This policy is designed to address medical guidelines that are appropriate for the majority of individuals with a particular disease, illness, or condition. Each person's unique clinical or other circumstances may warrant individual consideration, based on review of applicable medical records, as well as other regulatory, contractual and/or legal requirements.*

*Medical policies do not constitute medical advice, nor are they intended to govern the practice of medicine. They are intended to reflect Highmark's reimbursement and coverage guidelines. Coverage for services may vary for individual members, based on the terms of the benefit contract, and subject to the applicable laws of your state.*

*Highmark retains the right to review and update its medical policy guidelines at its sole discretion. These guidelines are the proprietary information of Highmark. Any sale, copying or dissemination of the medical policies is prohibited; however, limited copying of medical policies is permitted for individual use.*

#### **Discrimination is Against the Law**

*The Claims Administrator/Insurer complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. The Claims Administrator/Insurer does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex. The Claims Administrator/ Insurer:*

- *Provides free aids and services to people with disabilities 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 services to people whose primary language is not English, such as:*

- *Qualified interpreters*
- *Information written in other languages*

*If you need these services, contact the Civil Rights Coordinator.*

*If you believe that the Claims Administrator/Insurer 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: Civil Rights Coordinator, P.O. Box 22492, Pittsburgh, PA 15222, Phone: 1-866-286-8295, TTY: 711, Fax: 412-544-2475, email: [CivilRightsCoordinator@highmarkhealth.org](mailto:CivilRightsCoordinator@highmarkhealth.org). You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights 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>.*

*Insurance or benefit/claims administration may be provided by Highmark, Highmark Choice Company, Highmark Coverage Advantage, Highmark Health Insurance Company, First Priority Life Insurance Company, First Priority Health, Highmark Benefits Group, Highmark Select Resources, Highmark Senior Solutions Company or Highmark Senior Health Company, all of which are independent licensees of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield plans.*

ATTENTION: If you speak English, language assistance services, free of charge, are available to you. Call the number on the back of your ID card (TTY: 711).

ATENCIÓN: Si usted habla español, servicios de asistencia lingüística, de forma gratuita, están disponibles para usted. Llame al número en la parte posterior de su tarjeta de identificación (TTY: 711).

请注意：如果您说中文，可向您提供免费语言协助服务。

请拨打您的身份证背面的号码（TTY：711）。

CHÚ Ý: Nếu quý vị nói tiếng Việt, chúng tôi cung cấp dịch vụ hỗ trợ ngôn ngữ miễn phí cho quý vị. Xin gọi số điện thoại ở mặt sau thẻ ID của quý vị (TTY: 711).

알림: 한국어를 사용하시는 분들을 위해 무료 통역이 제공됩니다. ID 카드 뒷면에 있는 번호로 전화하십시오 (TTY: 711).

ATENSYON: Kung nagsasalita ka ng Tagalog, may makukuha kang mga libreng serbisyong tulong sa wika. Tawagan ang numero sa likod ng iyong ID card (TTY: 711).

ВНИМАНИЕ: Если вы говорите по-русски, вы можете воспользоваться бесплатными услугами языковой поддержки. Позвоните по номеру, указанному на обороте вашей идентификационной карты (номер для текст-телефонных устройств (TTY): 711).

تنبيه: إذا كنت تتحدث اللغة العربية، فهناك خدمات المعاونة في اللغة المجانية متاحة لك. اتصل بالرقم الموجود خلف بطاقة هويتك (جهاز الاتصال لذوي صعوبات السمع والنطق: 711).

ATTENTION: Si c'est créole que vous connaissez, il y a un certain service de langues qui est gratis et disponible pour vous-même. Composez le numéro qui est au dos de votre carte d'identité. (TTY: 711).

ATTENTION: Si vous parlez français, les services d'assistance linguistique, gratuitement, sont à votre disposition. Appelez le numéro au dos de votre carte d'identité (TTY: 711).

UWAGA: Dla osób mówiących po polsku dostępna jest bezpłatna pomoc językowa. Zadzwoń pod numer podany na odwrocie karty ubezpieczenia zdrowotnego (TTY: 711).

ATENÇÃO: Se a sua língua é o português, temos atendimento gratuito para você no seu idioma. Ligue para o número no verso da sua identidade (TTY: 711).

ATTENZIONE: se parla italiano, per lei sono disponibili servizi di assistenza linguistica a titolo gratuito. Contatti il numero riportato sul retro della sua carta d'identità (TTY: 711).

ACHTUNG: Wenn Sie Deutsch sprechen, steht Ihnen unsere fremdsprachliche Unterstützung kostenlos zur Verfügung. Rufen Sie dazu die auf der Rückseite Ihres Versicherungsausweises (TTY: 711) aufgeführte Nummer an.

注：日本語が母国語の方は言語アシスタンス・サービスを無料でご利用いただけます。IDカードの裏に明記されている番号に電話をおかけください (TTY: 711)。

توجه : اگر شما به زبان فارسی صحبت می کنید، خدمات کمک زبان، به صورت رایگان، در دسترس شماست. با شماره واقع در پشت کارت شناسایی خود ( TTY: 711 ) تماس بگیرید.