Tezspire® (Tezepelumab-Ekko)

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Instructions for Use

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Related Commercial Policies
- Provider Administered Drugs – Site of Care

Community Plan Policy
- Tezspire® (Tezepelumab-Ekko)

Coverage Rationale

See Benefit Considerations

This policy refers to Tezspire (tezepelumab-ekko) vial and pre-filled syringe for administration by a healthcare professional. Tezspire (tezepelumab-ekko) prefilled pen for self-administration is obtained under the pharmacy benefit.

Tezspire for provider administration is proven for add-on maintenance treatment for patients that meet the following criteria:

- For **initial therapy**, **all** of the following:
  - Diagnosis of severe asthma; **and**
  - Will be used as add-on maintenance therapy; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than12 months
- For **continuation of therapy**, **all** of the following:
  - Documentation of positive clinical response; **and**
  - Used in combination with an inhaled corticosteroid (ICS)-containing maintenance medication; **and**
  - Patient is not receiving Tezspire in combination with any of the following:
    - Anti-interleukin 5 therapy [e.g., Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab]
    - Anti-IgE therapy [e.g., Xolair (omalizumab)]
    - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]

    and
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no more than 12 months

Tezspire for provider administration is medically necessary when all of the following criteria is met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of severe asthma; **and**
  - Classification of asthma as uncontrolled or inadequately controlled as defined by at least **one** of the following:

- Poor symptom control (e.g., ACQ score consistently greater than 1.5 or ACT score consistently less than 20); **or**
- Two or more bursts of systemic corticosteroids for at least 3 days each in the previous 12 months; **or**
- Asthma-related emergency treatment (e.g., emergency room visit, hospital admission, or unscheduled physician's office visit for nebulizer or other urgent treatment); **or**
- Airflow limitation (e.g., after appropriate bronchodilator withhold FEV1 less than 80% predicted (in the face of reduced FEV1/FVC defined as less than the lower limit of normal); **or**
- Patient is currently dependent on maintenance therapy with oral corticosteroids for the treatment of asthma

and

- Used in combination with **one** of the following:
  - **One** maximally-dosed (appropriately adjusted for age) combination inhaled corticosteroid (ICS)/long-acting $beta_2$ agonist (LABA) product [e.g., Advair/AirDuo Respiclick (fluticasone propionate/salmeterol), Symbicort (budesonide/formoterol), Breo Ellipta (fluticasone furoate/vilanterol)]; **or**
  - Combination therapy including **both** of the following:
    - One maximally-dosed (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco®), mometasone furoate (Asmanex®), beclomethasone dipropionate (QVAR®)]; **and**
    - One additional asthma controller medication [e.g., LABA - olodaterol (Striverdi®) or indacaterol (Arcapta®), leukotriene receptor antagonist – montelukast (Singulair®), theophylline]

and

- Patient is not receiving Tezspire in combination with **any** of the following:
  - Anti-interleukin 5 therapy [e.g., Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab]
  - Anti-IgE therapy [e.g., Xolair (omalizumab)]
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]

and

- **One** of the following:
  - Physician attestation that the patient or caregiver is not competent or is physically unable to administer the Tezspire product FDA labeled for self-administration; **or**
  - Patient has documented history of severe hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, or hypotension) to Tezspire within the past 6 months and requires administration and direct monitoring by a healthcare professional; **or**
  - Patient is new to therapy with Tezspire and requires initial dose to be directly monitored by a healthcare professional before continued self-administration (Note: Authorization will be for 1 dose)

and

- Tezspire dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Tezspire is prescribed by a pulmonologist or allergist/immunologist; **and**
- Initial authorization will be for no more than 12 months

- For **continuation of therapy**, **all** of the following:
  - Documentation of a positive clinical response as demonstrated by at least **one** of the following:
    - Reduction in the frequency of exacerbations
    - Decreased utilization of rescue medications
    - Increase in percent predicted FEV1 from pretreatment baseline
    - Reduction in severity or frequency of asthma-related symptoms (e.g., wheezing, shortness of breath, coughing, etc.)

    and
  - Used in combination with an ICS-containing maintenance medication; **and**
  - Patient is not receiving Tezspire in combination with **any** of the following:
    - Anti-interleukin 5 therapy [e.g., Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab]
    - Anti-IgE therapy [e.g., Xolair (omalizumab)]
    - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]

    and
  - **One** of the following:
    - Physician attestation that the patient or caregiver is not competent or is physically unable to administer the Tezspire product FDA labeled for self-administration; **or**

- Patient has documented history of severe hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, or hypotension) to Tezspire within the past 6 months and requires administration and direct monitoring by a healthcare professional

and

- Tezspire dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

Applicable Codes

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

HCPCS Code	Description
J2356	Injection, tezepelumab-ekko, 1 mg

Diagnosis Code	Description
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.52	Severe persistent asthma with status asthmaticus
J82.83	Eosinophilic asthma

Background

Asthma is a common chronic inflammatory disease of the airways that affects an estimated 24 million adults and children. Although the disease is well controlled with inhaled therapy in most patients, approximately 1.2 to 2.4 million people have severe asthma (i.e., 5 to 10% of the asthma population) that is associated with substantial morbidity, mortality, and economic effects. Asthma has been divided into various clinical presentations or phenotypes. Key asthma phenotypes include allergic asthma, eosinophilic asthma, and non-eosinophilic asthma. Eosinophilic asthma is characterized by an increase in the blood and sputum eosinophil (EOS) levels; fractional exhaled nitric oxide (FeNO) also provides an indication of level of eosinophilic inflammation in the lung. In contrast, allergic asthma is characterized by a positive perennial aeroallergen skin test and/or increased levels of serum IgE. In current clinical practice, such phenotypic biomarkers are central to the management of severe, uncontrolled asthma as existing asthma biologic therapies are targeted at either eosinophilic or allergic asthma.[1] Approximately one-half of patients may present with overlapping or changing phenotypes, and almost 30% may not have a defined inflammatory pathway.[2]

Tezepelumab is a human monoclonal antibody that acts at the top of the inflammatory cascade by specifically binding TSLP, blocking TSLP from interacting with its receptor. Blocking TSLP with tezepelumab reduces downstream markers of inflammation, including blood EOS, immunoglobulin E (IgE), fractional exhaled nitric oxide (FeNO), interleukin 5 (IL-5), and interleukin 13 (IL-13).[3] Unlike other FDA-approved biologic therapies for severe asthma that target downstream inflammatory pathways and are indicated for specific patient phenotypes, because of its upstream activity early in the inflammatory cascade, tezepelumab is suitable for a broad spectrum of severe asthma patients irrespective of asthma phenotype.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare

diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

Tezepelumab is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.[4]

The efficacy of tezepelumab was established in two randomized, double-blind, placebo-controlled studies in 1,609 patients 12 years of age and older with severe asthma. PATHWAY was a 52-week dose-ranging study in which patients received tezepelumab-ekko 70 mg every 4 weeks, Tezspire 210 mg every 4 weeks, tezepelumab-ekko 280 mg every 2 weeks, or placebo. NAVIGATOR was a 52-week study in which patients received Tezepelumab 210 mg every 4 weeks or placebo. The primary endpoint in both studies was the rate of clinically significant asthma exacerbations measured over 52 weeks. Asthma exacerbations were defined as worsening of asthma requiring the use of or increase in oral or injectable corticosteroids for at least 3 days, or a single depo-injection of corticosteroids, and/or emergency department visits requiring use of oral or injectable corticosteroids and/or hospitalization. In PATHWAY, the annualized rate of asthma exacerbations was 0.20 with tezepelumab vs. 0.72 with placebo (rate ratio 0.29, 95% CI: 0.16, 0.51). In NAVIGATOR, the annualized rate of asthma exacerbations was 0.93 with tezepelumab vs. 2.10 with placebo (rate ratio 0.44, 95% CI: 0.37, 0.53). In NAVIGATOR, patients receiving tezepelumab experienced fewer exacerbations than those receiving placebo regardless of baseline levels of blood eosinophils or fractional exhaled nitric oxide (FeNO). Similar results were seen in PATHWAY.

Tezepelumab was also evaluated in a randomized, double-blind, placebo-controlled clinical study in 150 adult patients with severe asthma requiring treatment with daily oral corticosteroids (OCS). Patients received tezepelumab 210 mg every 4 weeks or placebo. The primary endpoint was categorized percent reduction from baseline of the final OCS dose at week 48 (≥ 90% reduction, ≥ 75% to < 90% reduction, ≥ 50% to < 75% reduction, > 0% to < 50% reduction, and no change or no decrease in OCS), while maintaining asthma control. Tezspire did not demonstrate a statistically significant reduction in maintenance OCS dose vs. placebo (cumulative odds ratio 1.28, 95% CI: 0.69, 2.35).

Professional Societies

Global Initiative for Asthma

The Global Initiative for Asthma (GINA, 2023) defines uncontrolled, difficult-to-treat and severe asthma as follows[1]:

- Uncontrolled asthma is asthma with poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma) and/or frequent exacerbations (≥ 2/year) requiring OCS, or serious exacerbations (≥ 1/year) requiring hospitalization.
- Difficult-to-treat asthma is asthma that is uncontrolled despite prescribing of medium- or high-dose ICS with a second controller (usually a LABA) or maintenance OCS, or that requires high-dose treatment to maintain good symptom control and reduce the risk of exacerbations.
- Severe asthma is asthma that is uncontrolled despite adherence with maximal optimized high-dose ICS-LABA treatment and management of contributory factors, or that worsens when high-dose treatment is decreased. Asthma is not classified as severe if it markedly improves when contributory factors such as inhaler technique and adherence are addressed.

The Global Initiative for Asthma (GINA, 2023) recommends add-on biologic therapy for treatment of adults, adolescents and children with uncontrolled severe asthma despite optimized maximal therapy as follows:

- Add-on anti-immunoglobulin E (anti-IgE) treatment (omalizumab) for patients aged ≥ 6 years) with severe allergic asthma (Evidence A).
- Add-on anti-interleukin 5/5R treatment (subcutaneous mepolizumab for patients aged ≥ 6 years; intravenous reslizumab for ages ≥ 18 years; subcutaneous benralizumab for ages ≥ 12 years) with severe eosinophilic asthma (Evidence A).
- Add-on anti-interleukin-4R α treatment (subcutaneous dupilumab) for patients aged ≥ 6 years with severe eosinophilic/Type 2 asthma, or for adults or adolescents requiring treatment with maintenance OCS (Evidence A).
- Add-on anti-thymic stromal lymphopoietin (anti-TSLP) treatment (subcutaneous tezepelumab for patients aged ≥ 12 years with severe asthma (Evidence A).

The Global Initiative for Asthma (GINA, 2023) recommends that low dose oral corticosteroids (≤ 7.5 mg/day prednisone equivalent) should only be considered as last resort in adult patients with severe asthma with poor symptom control and/or frequent exacerbations despite good inhaler technique and adherence with Step 5 treatment, and after exclusion of other contributory factors and other add-on treatments including biologics where available and affordable. (Evidence D). Oral corticosteroids are often associated with substantial side effects (Evidence A).

Institute for Clinical and Economic Review (ICER)

On November 4, 2021, the Institute for Clinical and Economic Review (ICER) released a clinical report entitled, "Tezepelumab for Severe Asthma." ICER recommendations are as follows: [5]

- ICER rates the net health benefit of tezepelumab added to standard-of-care therapy without biologics, compared with standard-of-care therapy alone in adults and adolescents with severe, uncontrolled asthma as "Comparable or Better" (C++).
- ICER judges the current body of evidence tezepelumab compared with dupilumab in patients with eosinophilic asthma as "Insufficient" (I). In the subgroup of patients with eosinophilic asthma, reductions in AAER and (small) improvements in daily symptoms and quality of life seem similar to those seen with dupilumab. Dupilumab has substantially more evidence on long-term safety.
- ICER judges the current body of evidence for tezepelumab compared with omalizumab in patients with allergic asthma as "insufficient" (I).
- ICER rates the treatment of patients with steroid-dependent asthma as "Comparable or Inferior" (C-) to treatment with dupilumab.

European Respiratory Society (ERS)/American Thoracic Society (ATS)

The first European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines on severe asthma were published in 2014. Severe asthma was defined as that which requires treatment with high-dose ICSs plus a second controller (or systemic corticosteroids) to prevent progression to uncontrolled disease status or continuing uncontrolled disease status despite this therapy.[3] Emphasis was placed on the necessity to confirm the diagnosis of asthma and exclude other conditions that may mimic asthma. In addition, the guidelines recognized that severe asthma is a heterogeneous condition consisting of phenotypes such as severe eosinophilic asthma, and specific recommendations were made on the use of sputum eosinophil count and exhaled nitric oxide fraction (F_{ENO}) to guide therapy. Recommendations were also made for the use of methotrexate, macrolide antibiotics, antifungal agents, bronchial thermoplasty and the anti-IgE antibody omalizumab in severe asthma.

In 2020, the European Respiratory Society (ERS)/American Thoracic Society (ATS) published updated guidelines for the management of asthma.[23] Six specific and important questions were formulated using the PICO (Patient population, Intervention, Comparison and Outcome) format. The GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach was used to assess the strength of evidence and develop recommendations. These recommendations are summarized below:

- An anti-interleukin (IL)-5 and anti-IL-5 receptor α for severe uncontrolled adult eosinophilic asthma phenotypes
- A blood eosinophil cut-point ≥ 150 μL^{-1} to guide anti-IL-5 initiation in adult patients with severe asthma
- Specific eosinophil (≥ 260 μL^{-1}) and exhaled nitric oxide fraction (≥ 19.5 ppb) cut-offs to identify adolescents or adults with the greatest likelihood of response to anti-IgE therapy
- Inhaled tiotropium for adolescents and adults with severe uncontrolled asthma despite Global Initiative for Asthma (GINA) step 4-5 or National Asthma Education and Prevention Program (NAEPP) step 5 therapies
- A trial of chronic macrolide therapy to reduce asthma exacerbations in persistently symptomatic or uncontrolled patients on GINA step 5 or NAEPP step 5 therapies, irrespective of asthma phenotype
- Anti-IL-4/13 for adult patients with severe eosinophilic asthma and for those with severe corticosteroid-dependent asthma regardless of blood eosinophil levels

U.S. Food and Drug Administration (FDA)

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

Tezspire (tezepelumab) is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. Tezepelumab is not indicated for the relief of acute bronchospasm or status asthmaticus.[1]

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for Tezspire® (tezepelumab-ekko). Local Coverage Determinations (LCDs)/Local Coverage Articles (LCAs) do not exist at this time.

In general, Medicare may cover outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.
(Accessed March 1, 2023)

References

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3. Corren J, Ziegler SF. TSLP: from allergy to cancer. Nat Immunol. 2019;20(12):1603-1609. doi:10.1038/s41590-019-0524-9.
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6. Holguin F, Cardet JC, Chung KF, Diver S, Ferreira DS, Fitzpatrick A, Gaga M, Kellermeyer L, Khurana S, Knight S, McDonald VM, Morgan RL, Ortega VE, Rigau D, Subbarao P, Tonia T, Adcock IM, Bleecker ER, Brightling C, Boulet LP, Cabana M, Castro M, Chanez P, Custovic A, Djukanovic R, Frey U, Frankemölle B, Gibson P, Hamerlijnck D, Jarjour N, Konno S, Shen H, Vitary C, Bush A. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020 Jan 2;55(1):1900588. doi: 10.1183/13993003.00588-2019. PMID: 31558662.

Policy History/Revision Information

Date	Summary of Changes
10/01/2023	**Coverage Rationale** • Added language to indicate this policy refers to Tezspire (tezepelumab-ekko) vial and pre-filled syringe for administration by a healthcare professional; Tezspire (tezepelumab-ekko) prefilled pen for self-administration is obtained under the pharmacy benefit • Replaced language indicating: ○ "Tezspire is proven for add-on maintenance treatment [when the listed criteria are met]" with "Tezspire *for provider administration* is proven for add-on maintenance treatment [when the listed criteria are met]" ○ "Tezspire is medically necessary when [the listed] criteria are met" with "Tezspire *for provider administration* is medically necessary when [the listed] criteria are met" • Replaced reference to "inhaled corticosteroid (ICS)-containing *controller* medication" with "inhaled corticosteroid (ICS)-containing *maintenance* medication" • Revised medical necessity criteria: ***Initial Therapy*** ○ Added criterion requiring **one** of the following: ▪ Physician attestation that the patient or caregiver is not competent or is physically unable to administer the Tezspire product FDA labeled for self-administration ▪ Patient has documented history of severe hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, or hypotension) to Tezspire within the past 6 months and requires administration and direct monitoring by a healthcare professional

Date	Summary of Changes
	▪ Patient is new to therapy with Tezspire and requires initial dose to be directly monitored by a healthcare professional before continued self-administration (authorization will be for 1 dose) ○ Removed criterion requiring **one** of the following: ▪ Both of the following: – Tezspire will be used to treat eosinophilic asthma – History of failure, contraindication, or intolerance to a 4-month trial of both of the following: ● Anti-interleukin 5 therapy [e.g., Nucala (mepolizumab), Fasenra (benralizumab)] ● Anti-interleukin 4 [e.g., Dupixent (dupilumab)] ▪ Both of the following: – Tezspire will be used to treat persistent allergic asthma – History of failure, contraindication, or intolerance to a 4-month trial of Xolair (omalizumab) ▪ Both of the following: – Tezspire will be used to treat oral corticosteroid dependent asthma – History of failure, contraindication, or intolerance to a 4-month trial of Dupixent (duplimab) ▪ Patient's asthma is not of the eosinophilic, allergic or oral corticosteroid dependent phenotype ▪ Patient is currently on Tezspire ○ Replaced criterion requiring: ▪ "Tezspire is used in combination with one *high*-dose (appropriately adjusted for age) ICS product" with "Tezspire is used in combination with one *maximally*-dosed (appropriately adjusted for age) ICS product" ▪ "Initial authorization will be for no more than ***6*** months" with "initial authorization will be for no more than ***12*** months" ***Continuation of Therapy*** ○ Added criterion requiring **one** of the following: ▪ Physician attestation that the patient or caregiver is not competent or is physically unable to administer the Tezspire product FDA labeled for self-administration ▪ Patient has documented history of severe hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, or hypotension) to Tezspire within the past 6 months and requires administration and direct monitoring by a healthcare professional **Supporting Information** • Updated *Clinical Evidence*, *CMS*, and *References* sections to reflect the most current information • Archived previous policy version 2023D00110F

Instructions for Use

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

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

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