

# Tezspire™ (Tezepelumab-Ekko)

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[➔ Instructions for Use](#)

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<b>Related Commercial Policies</b>
<ul style="list-style-type: none"> <li><a href="#">Provider Administered Drugs – Site of Care</a></li> </ul>
<b>Community Plan Policy</b>
<ul style="list-style-type: none"> <li><a href="#">Tezspire™ (Tezepelumab-Ekko)</a></li> </ul>

## Coverage Rationale

[➔ See Benefit Considerations](#)

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

- For initial therapy, both of the following:
  - Diagnosis of severe asthma; and
  - Will be used as add-on maintenance therapy
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Initial authorization will be for no more than 6 months.
- For continuation of therapy, all of the following:
  - Documentation of positive clinical response; and
  - Used in combination with an inhaled corticosteroid (ICS)-containing controller medication; and
  - Patient is not receiving Tezspire in combination with any of the following:
    - Anti-interleukin 5 therapy [e.g., Cinqair (reslizumab), Fasentra (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 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<sub>2</sub> 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 high-dose (appropriately adjusted for age) ICS product [e.g., ciclesonide (Alvesco<sup>®</sup>), mometasone furoate (Asmanex<sup>®</sup>), beclomethasone dipropionate (QVAR<sup>®</sup>)]; and
    - One additional asthma controller medication [e.g., LABA - olodaterol (Striverdi<sup>®</sup>) or indacaterol (Arcapta<sup>®</sup>), leukotriene receptor antagonist – montelukast (Singulair<sup>®</sup>), theophylline]
- and
- One of the following (for Medicare reviews, refer to the [CMS](#) section\*):
  - Both of the following:
    - Tezspire will be used to treat eosinophilic asthma; and
    - History of failure, contraindication, or intolerance to a 4-month trial of both of the following:
      - Anti-interleukin 5 therapy [e.g., Nucala (mepolizumab), Fasentra (benralizumab)]
      - Anti-interleukin 4 [e.g., Dupixent (dupilumab)]; or
  - Both of the following:
    - Tezspire will be used to treat persistent allergic asthma; and
    - History of failure, contraindication, or intolerance to a 4-month trial of Xolair (omalizumab); or
  - Both of the following:
    - Tezspire will be used to treat oral corticosteroid dependent asthma; and
    - History of failure, contraindication, or intolerance to a 4-month trial of Dupixent (dupilumab); or
  - Patient's asthma is not of the eosinophilic, allergic or oral corticosteroid dependent phenotype; or
  - Patient is currently on Tezspire
- and
- Patient is not receiving Tezspire in combination with any of the following:
  - Anti-interleukin 5 therapy [e.g., Cinqair (reslizumab), Fasentra (benralizumab), Nucala (mepolizumab)]
  - Anti-IgE therapy [e.g., Xolair (omalizumab)]
  - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
- 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 6 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 controller medication; and
  - Patient is not receiving Tezspire in combination with any of the following:
    - Anti-interleukin 5 therapy [e.g., Cinqair (reslizumab), Fasentra (benralizumab), Nucala (mepolizumab)]
    - Anti-IgE therapy [e.g., Xolair (omalizumab)]
    - Anti-interleukin 4 therapy [e.g., Dupixent (dupilumab)]
  - 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.<sup>1</sup> Approximately one-half of patients may present with overlapping or changing phenotypes, and almost 30% may not have a defined inflammatory pathway.<sup>2</sup>

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).<sup>3</sup> 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.

## Proven

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

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 ( $\geq 90\%$  reduction,  $\geq 75\%$  to  $< 90\%$  reduction,  $\geq 50\%$  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, 2022) recommends that for Step 5 treatment, adults and adolescents, may be treated with Fasenra (benralizumab), Dupixent (dupilumab), Nucala (mepolizumab), Xolair (omalizumab), Cinquair (reslizumab), or Tezspire (tezepelumab) as follows:<sup>1</sup>

- Refer for expert assessment, phenotyping, and add-on therapy. Patients of any age with persistent symptoms or exacerbations despite correct inhaler technique and good adherence with Step 4 treatment and in whom other controller options have been considered, should be referred to a specialist with expertise in investigation and management of severe asthma (Evidence D).
- Add-on treatment for moderate or severe allergic asthma that is uncontrolled on Step 4-5 treatment: anti-immunoglobulin E (subcutaneous omalizumab for patients  $\geq 6$  years) (Evidence A).
- Add-on treatment for severe eosinophilic asthma that is uncontrolled on Step 4-5 treatment: anti-interleukin 5/5R treatment (subcutaneous mepolizumab for patients aged  $\geq 6$  years; intravenous reslizumab for ages  $\geq 18$  years; subcutaneous benralizumab for ages  $\geq 12$  years; or subcutaneous dupilumab for ages  $\geq 6$  years) (Evidence A)
- Add-on treatment for severe Type 2 asthma or requiring treatment with maintenance OCS: anti-interleukin-4R  $\alpha$  treatment (subcutaneous dupilumab for ages  $\geq 6$  years) (Evidence A)
- Add-on treatment for severe asthma that is uncontrolled on Step 4-5 treatment: anti-thymic stromal lymphopoietin (anti-TSLP) treatment (subcutaneous tezepelumab for ages  $\geq 12$  years) (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:<sup>5</sup>

- 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.

## 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.<sup>1</sup>

## Centers for Medicare and Medicaid Services (CMS)

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

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 May 13, 2022)

\*Preferred therapy criteria are not applicable for Medicare Advantage members.

## References

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2022. Available at <http://www.ginasthma.org>. Accessed August 18, 2022.
2. Tran TN, Zeiger RS, Peters SP, et al. Overlap of atopic, eosinophilic, and TH2-high asthma phenotypes in a general population with current asthma. *Ann Allergy Asthma Immunol*. 2016;116(1):37-42. doi:10.1016/j.anai.2015.10.027.
3. Corren J, Ziegler SF. TSLP: from allergy to cancer. *Nat Immunol*. 2019;20(12):1603-1609. doi:10.1038/s41590-019-0524-9.
4. Tezspire™ [package insert]. Thousand Oakes, CA: Amgen Inc.; December 2021.
5. Institute for Clinical and Economic Review (ICER). Tezepelumab for Severe Asthma. November 4, 2021. Available at [ICER | Working Towards Fair Pricing, Fair Access, & Future Innovation](#). Accessed December 22, 2021.

## Policy History/Revision Information

Date	Summary of Changes
01/01/2023	<p><b>Coverage Rationale</b></p> <ul style="list-style-type: none"><li>● Revised medical necessity criteria for initial therapy; added criterion to allow coverage when the patient’s asthma is not of the eosinophilic, allergic, or oral corticosteroid dependent phenotype</li></ul> <p><b>Supporting Information</b></p> <ul style="list-style-type: none"><li>● Archived previous policy version 2022D00110E</li></ul>

## 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<sup>®</sup> 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.