Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCRES018.0624	**RESPIRATORY AGENTS** **TEZSPIRE®** (tezepelumab-ekko injection)
Effective Date: 8/1/2024	**Review/Revised Date**: 04/23, 05/23, 08/23, 05/24 (snm)
Original Effective Date: 07/22	**P&T Committee Meeting Date**: 06/22, 04/23, 08/23. 06/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
1. For patients initiating therapy, all the following criteria must be met:
    a. In the past three months, patient is adherent to treatment with maximally tolerated doses of both of the following, unless patient has an intolerance or contraindication to all therapies (This may be verified by pharmacy claims information):
        i. Inhaled corticosteroid
        ii. One of the following:
            1) A long-acting inhaled beta 2-agonist (LABA)
            2) A leukotriene receptor antagonist (LTRA)
            3) A long-acting muscarinic antagonist (LAMA)
    b. Inadequate asthma control despite above therapy, defined as one of the following:
        i. Asthma Control Test (ACT) score less than 20 or Asthma Control Questionnaire (ACQ) score greater than or equal to 1.5
        ii. At least two exacerbations requiring oral systemic corticosteroids in the last 12 months
        iii. At least one exacerbation requiring hospitalization, emergency room or urgent care visit in the last 12 months
        iv. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered

v. Baseline (prior to therapy with the requested agent) Forced Expiratory Volume (FEV1) that is less than 80% of predicted

2. For patients established on therapy for asthma: Response to therapy indicating improvement or stabilization of condition

EXCLUSION CRITERIA:
Concurrent use with anti-IL5 (such as mepolizumab, reslizumab, benralizumab), anti-IgE, anti-TSLP (such as tezepelumab), or anti-IL4 (such as dupilumab) monoclonal antibodies

AGE RESTRICTIONS:
For all indications, the patient's age must be within FDA labeling for the requested indication

PRESCRIBER RESTRICTIONS:
For initial authorization and reauthorization, must be prescribed by or in consultation with an asthma specialist (such as a pulmonologist, immunologist, or allergist)

COVERAGE DURATION:
Authorization will be approved until no longer eligible with the plan, subject to formulary and/or benefit changes. Note that the approval of the prior authorization for the medication is for self-administration at home, after the monitoring period allowed at the provider's office, as outlined in clinical policy Self-Administered Drugs ORPTCOTH042.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Tezepelumab-ekko (Tezspire®) is a human monoclonal antibody thymic stromal lymphopoietin (TSLP) blocker, which reduces markers inflammation, such as blood eosinophils, airway submucosal eosinophils, interleukin-5 (IL-5), and IL-13.

Per package labeling, the vial and pre-filled syringe formulations are intended for administration by a healthcare provider. The pre-filled pen formulation can be administered by patients/caregivers or healthcare providers.

FDA APPROVED INDICATIONS:
Add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.

- Limitations of Use: not indicated for the relief of acute bronchospasm or status asthmaticus.

POSITION STATEMENT:
Global Initiative for Asthma (GINA) 2023 guidelines define severe asthma as that which is not controlled with high-dose ICS-LABA therapy, despite good adherence to therapy. It can also be patients with symptoms that return/worsen when the dose of ICS-LABA therapy is lowered. The management of severe asthma should be based on the phenotype and add-on treatments may include long-acting muscarinic antagonists (LAMA), leukotriene receptor antagonists (LTRA), low-dose azithromycin, and/or biologics.[4]

Alternative biologic therapy options:

Drug	Dosing	Mechanism	Indication
Omalizumab (Xolair®)	75-375 mg SC Q2W or Q4W	Anti-IgE	Age ≥6 years with moderate to severe persistent asthma testing positive for perennial aeroallergen whose symptoms are inadequately controlled with ICS
Dupilumab (Dupixent®)	200-300 mg SC Q2W	Anti-IL-4Rα	Age ≥12 years with moderate to severe asthma with an eosinophilic phenotype or with OCS-dependent asthma
Mepolizumab (Nucala®)	100 mg SC Q4W	Anti-IL-5	Age ≥6 years with severe asthma with an eosinophilic phenotype
Benralizumab (Fasenra®)	30 mg SC Q4W for 3 doses, then Q8W	Anti-IL-5Rα	Age ≥12 years with severe asthma with an eosinophilic phenotype
Reslizumab (Cinqair®)	3 mg/kg IV infusion Q4W	Anti-IL-5	Age ≥18 years with severe asthma with an eosinophilic phenotype

Clinical Trials for tezepelumab-ekko:
NAVIGATOR (PubMed ID #NCT03347279)[5]

- R, DB, PC, phase 3 study
- Study Duration: 52 weeks

- Patient population: Patients (N=1061) between 12 to 80 years of age with physician diagnosed asthma for at least 12 months, taking a controller regimen of medium/high dose ICS for at least 12 months plus one additional controller for at least three months. In addition, patients must have had severe disease, defined as one of the following in the 12 months prior to informed consent:
    - History of at least two asthma exacerbations that led to hospitalization
    - An emergency department visit that resulted in the use of systemic glucocorticoids for at least three consecutive days
- Key Exclusion criteria: patients with any clinically important pulmonary disease other than asthma or pulmonary or systemic diseases, other than asthma, that are associated with elevated peripheral eosinophil count.
- Intervention: Randomized in 1:1 ratio to TEZ 210 mg (N=529) and placebo (N=532) subcutaneously every four weeks for 52 weeks
- Primary endpoint: AAER over 52 weeks
- Results:
    - Baseline characteristics: Mean age 50 years; 36.5% male sex; 62.2% white race, 27.9% Asian, 5.8% Black Americans; 75% on high dose ICS, 9% on OCS, 50% on LABA
    - Efficacy:
        - TEZ treatment reduced AAER by 56% compared to placebo group; ARR 1.17 and NNT 1.

	TEZ	Placebo	Rate Ratio
AAER	0.93	2.10	0.44 (0.37-0.53); P<0.001

        - TEZ group had a greater improvement in baseline prebronchodilator FEV1 (0.23 vs. 0.09 liters; 95% CI, 0.08 to 0.18; P<0.001). The minimum clinically important difference (MCID) is 0.1 liter
        - TEZ group had improvement in other symptom scores like Asthma Control Questionnair-6 (-1.55 vs. -1.22; 95% CI, -0.46 to -0.20; P<0.001), Asthma Quality of Life Questionnaire (1.49 vs. 1.15; 95% CI, 0.20 to 0.47; P<0.001), and Asthma Symptom Dairy (-0.71 vs. -0.59; 95% CI, -0.19 to -0.04; P=0.002), but did not meet MCID of at least 0.5 points
        - Based on subgroup analysis, patients with eosinophil count at least 300 cells/µl (rate ratio, 0.30, 95% CI, 0.22 to 0.40) at baseline had a greater reduction in AAER compared to eosinophil count <300 cells/µl (rate ratio, 0.59; 95% CI, 0.46 to 0.75; P<0.001)

    - Safety: There was no meaningful difference in adverse events between the two groups. The most common adverse events were nasopharyngitis, upper respiratory tract infection, headache, and asthma.
        - The incidence of severe infections such as pneumonia and diverticulitis did not differ between two groups
        - Two deaths were reported (heart failure and unknown cause) in the placebo group
- GRADE evidence rating: Moderate
    - Strengths: Randomized, double-blind, multicenter trial; well-balanced patient characteristics
    - Limitations: Reduced generalizability due to under-enrollment of ethnic minorities (Black Americans have a higher prevalence of severe asthma than White Americans, but represent very small proportion of patients in this trial); placebo controlled trial; Manufacturer coordinated data management and performed statistical analysis; Small number (9.4%) of patients were on oral corticosteroids (OCS)

SOURCE (PubMed ID: 35364018)[6]

- R, DB, PC, Phase 3 study
- Study Duration: 48 weeks
- Patient population: Patients (N=150) 18-80 years of age with physician diagnosed asthma for at least 12 months on controller regimen including all the following: 1) medium/high dose ICS for at least 12 months (patients on medium-dose ICS were required to increase to a high dose for at least three months before screening), 2) LABA for at least three months, and 3) OCS for at least six months. Patients must have had severe asthma, defined as one of the following in the 12 months prior to screening:
    - History of at least two asthma exacerbations that led to hospitalization
    - An emergency department visit that resulted in the use of systemic glucocorticoids for at least three consecutive days
    - Need for use of systemic corticosteroids for at least three consecutive days
- Key exclusion criteria included any clinically important pulmonary disease, other than asthma, associated with high peripheral eosinophil counts, any clinically significant infection including helminth or parasitic infections.
- Intervention: 1:1 randomization into TEZ 210 mg SC every four weeks and placebo SC every four weeks, after a 2-week screening/run-in followed by an OCS optimization phase of up to eight weeks. Eligible patients were then randomized for the treatment period with the following phases:
    - Induction (four weeks of stable OCS dose)
    - Dose-reduction (36 weeks, protocol-driven dose reduction)
    - Maintenance (eight weeks without any dose reductions)

- Primary endpoint: Percent reduction from baseline in the daily OCS dose at week 48 while not losing asthma control
    - Key secondary endpoint: AAER over the treatment period
- Results:
    - Baseline Characteristics: Mean age 54 years, 37% male sex, 84% white race (1% Black American); 99% on high dose ICS, 100% on OCS; Median baseline eosinophil count 200-215 cells/µL, FeNO 26-28 ppb, IgE 109-123 mg/L
    - Efficacy:
        - The study did not meet the primary endpoint with no statistical difference in reduction of daily OCS dose between TEZ and placebo [Odds Ratio (95% CI): 1.28 (0.69, 2.35); P=0.434].

Reduction from baseline daily OCS dose	TEZ 210 mg n (%)	Placebo (N=76)
≥90% to 100% reduction	40 (54.1)	35 (46.1)
≥75% to <90% reduction	5 (6.8)	4 (5.3)
≥50% to <75% reduction	10 (13.5)	14 (18.4)
>0% to <50% reduction	5 (6.8)	9 (11.8)
No change or any increase	14 (18.9)	14 (18.4)

        - In subgroup analysis, the odd ratio favored those with higher baseline levels of blood eosinophils (≥150 cells/µL), higher FeNO (≥25 ppb), positive allergic status, lower daily OCS (≤10 mg/day), but these findings were difficult to interpret due to the small number of subjects.
        - The reduction in AAER was a secondary outcome, and it did show a reduction in subjects treated with TEZ compared to placebo, but it was not statistically significant.
            - TEZ: 1.38 (.98-1.95
            - Placebo: 2.00 (1.46-2.74)
            - Rate ratio 0.69 (95% CI 0.44–1.09)
    - Safety: No difference in adverse events between two groups.
        - The most common adverse events reported were nasopharyngitis, upper respiratory tract infection, bronchitis, and oral candidiasis.
- GRADE evidence rating: Low
    - Strengths: Randomized trial, well-balanced patient characteristics
    - Limitations: Small sample size (N=150); Reduced generalizability due to under-enrollment of ethnic minorities (Black Americans have a higher prevalence of severe asthma than White Americans, but represent very small proportion of patients in this trial); Protocol amendment to increase

number of subjects enrolled to provide more power to reject the null hypothesis

Cost-effectiveness studies:[7]

Institute for Clinical and Economic Review (ICER) conducted a review of tezepelumab for Severe Asthma in December 2021. Summary of conclusions:

- Tezepelumab is considered "Comparable or Better" than placebo therapy in patients with severe, uncontrolled asthma
    - Tezepelumab reduced exacerbation rates in patients with severe asthma compared to placebo.
    - It also exhibited trends towards improved symptom scores but did not meet minimal clinically important differences versus placebo.
    - Tezepelumab showed similar improvement in symptom scores and reduction in AAER in patients with and without eosinophilic asthma
- There was insufficient evidence to rate tezepelumab against dupilumab in patients with eosinophilic asthma or omalizumab in patients with allergic asthma
- Tezepelumab did not show a benefit for reducing oral corticosteroid use in adult patients with severe steroid-dependent asthma and was rated as "Comparable or Inferior" to dupilumab
- Of note, the report outlines that severe asthma is more common in Black Americans, but the clinical trials did not include a robust Black population to determine a true effect in these patients
- Tezepelumab treatment likely not considered cost-effective in the US market

REFERENCE/RESOURCES:

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3. Tezspire In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed May 11, 2024.
4. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention (2023 Update). Available at: http://www.ginasthma.org. Accessed on May 11, 2024.
5. Menzies-Gow, Andrew et al. "Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma." *NEJM. 2021:* 384(19):1800-1809. doi:10.1056/NEJMoa2034975
6. Wechsler M, Menszies-Gow A, Brightling CE, et al. Evaluation of the oral corticosteroid-sparing effect of tezepelumab in adults with oral corticosteroid-dependent asthma (SOURCE): a randomised, placebo-controlled, phase 3

study. *Lancet Respir Med. 2022 Mar 29;S2213-2600(21)00537-3.*
7. Rind DM, McQueen RB, Herron-Smith S, et al. Tezepelumab for Severe Asthma; Final Report. Institute for Clinical and Economic Review, December 16, 2021. https://icer.org/wp-content/uploads/2021/12/ICER_Severe-Asthma_Key-Policy-Recommendations_121621.pdf Accessed May 11, 2024.
8. Providence Health Plan Pharmacy Prior Authorization Policy and Criteria ORPTCOTH042. Self-Administered Drugs (SAD). Last revised October 2023.

CPT/HCPCS CODES

Brand Name	Generic Name	HCPCS Code
Tezspire	Tezepelumab-ekko	J2356