Medical Policy Bulletin

Title:
Tezepelumab-ekko (Tezspire®)
Policy #:
MA08.144b

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

INITIAL THERAPY
Tezepelumab-ekko (Tezspire), administered by subcutaneous (SC) injection by a healthcare professional provider, is considered medically necessary and, therefore, covered for the add-on maintenance treatment of adult and pediatric individuals aged 12 years and older with **both** of the following:

- Severe asthma with **all** of the following (background asthma therapy must continue during treatment with tezepelumab-ekko [Tezspire]):
    - Pre-bronchodilator forced expiratory volume in 1 second (FEV1) below 80 percent predicted in adults or below 90 percent in adolescents
    - Regular treatment with medium or high-dose inhaled corticosteroids (ICS) (unless a contraindication or intolerance exists) and at least one additional asthma controller (e.g., long-acting beta2 agonist [LABA] inhaler, long-acting muscarinic antagonist [LAMA] inhaler, leukotriene modifier) for 3 months or more
    - With or without oral corticosteroids
- Have a history of **one** of the following:
    - Two or more asthma exacerbations requiring oral or injectable corticosteroid treatment
    - One asthma exacerbation resulting in hospitalization in the past 12 months

CONTINUATION THERAPY
Tezepelumab-ekko (Tezspire), administered by subcutaneous (SC) injection by a healthcare professional provider, is considered medically necessary and, therefore, covered for continuation therapy for the add-on treatment of severe

asthma when there is documentation confirming **any** of the following:

- Clinical improvement in the individual's symptoms of asthma
- Increase in FEV1 value from pretreatment baseline
- Decreased utilization of rescue medication

EXPERIMENTAL/INVESTIGATIONAL

All other uses of tezepelumab-ekko (Tezspire) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the drug. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial of the drug.

Guidelines

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, tezepelumab-ekko (Tezspire) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Tezepelumab-ekko (Tezspire) was approved by the FDA on December 17, 2021, for the add-on maintenance treatment of adult and pediatric individuals aged 12 years and older with severe asthma.

PEDIATRIC USE
The safety and effectiveness of tezepelumab-ekko (Tezspire) have been established in pediatric individuals 12 years and older for the add-on maintenance treatment of severe asthma.

The safety and effectiveness of tezepelumab-ekko (Tezspire) have not been established for any indication in pediatric individuals less than 12 years of age.

Description

Tezepelumab-ekko (Tezspire) is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody immunoglobulin (IgG2) lambda that binds to human TSLP and blocks its interaction with the heterodimeric TSLP receptor. TSLP is a cytokine mainly derived from epithelial cells and occupies an upstream position in the asthma inflammatory cascade. Airway inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, macrophages, lymphocytes, type 2 innate lymphoid cells [ILC2]) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in airway inflammation. Blocking TSLP with tezepelumab-ekko (Tezspire) reduces biomarkers and cytokines associated with inflammation including blood eosinophils, airway submucosal eosinophils, IgE, fractional exhaled nitric oxide (FeNO), interleukin-5 (IL-5), and IL-13; however, the mechanism of tezepelumab-ekko (Tezspire) action in asthma has not been definitively established.

PEER-REVIEWED LITERATURE

SUMMARY

Tezepelumab-ekko (Tezspire) was studied in a multicentre, phase 2, randomized, placebo-controlled, parallel-group, double-blind, dose-ranging clinical trial (Corren et al., 2017; NCT02054130; PATHWAY). Eligibility criteria included current nonsmoker for six months or more, poorly-controlled asthma despite treatment with a long-acting beta agonist (LABA) and either medium (250 to 500 µg per day of inhaled fluticasone [or equivalent]) or high (>500 µg per day of fluticasone [or equivalent]) for at least six months or longer, a history of at least two asthma exacerbations requiring treatment with systemic steroids or one severe exacerbation resulting in hospitalization in the preceding 12 months, and a prebronchodilator forced expiratory volume in 1 second (FEV1) of at least 40 percent but no more than 80 percent of the predicted normal value. Individuals were randomly assigned in a 1:1:1:1 ratio to one of three different dosages (70 mg every four weeks, 210 mg every four weeks, 280 mg every two weeks) of tezepelumab-ekko (Tezspire) subcutaneously (SC) or placebo. Baseline asthma treatment medications were maintained throughout the study. The primary endpoint was the annualized rate of asthma exacerbations at one year. One of the secondary endpoints included changes in FEV1 values. Of the 550 individuals randomized equally into the four groups, the annualized rates of asthma exacerbations at one year were 0.27, 0.20, 0.23, and 0.72 for the low dose, medium dose, high dose, and placebo groups respectively. This demonstrated a 62 percent (90 percent confidence interval [CI], 42 to 75; p<0.001), 71 percent (90 percent CI, 54 to 82; p<0.001), and 66 percent (90 percent CI 47 to 79; p<0.001) improvement in the respective dosage groups versus placebo. The asthma exacerbation rates did not vary irrespective of baseline eosinophil count or other biomarkers. Improvement in FEV1 values as compared to placebo were 0.12 liters (95 percent CI, 0.02 to 0.22; p=0.015), 0.13 liters (95 percent CI, 0.03 to 0.23; p=0.009), and 0.15 liters (95 percent CI, 0.05 to 0.25; p=0.002) in the low dose, medium dose, and high dose groups respectively. The treatment effects on these values were seen as early as four weeks and were sustained for the remainder of the clinical trial. There were also substantial and continued decreases in the eosinophil and FeNO levels in all the tezepelumab-ekko (Tezspire) treatment groups as early as four weeks.

Tezepelumab-ekko (Tezspire) was studied in a multicentre, phase 3, randomized, placebo controlled, parallel group, double-blind clinical trial (Menzies-Gow et al., (2020; NCT03347279; NAVIGATOR). Eligibility criteria included individuals aged 12 years and older with severe, uncontrolled asthma who had received medium to high-dose inhaled corticosteroids (ICS) for at least three months alone with at least one other asthma-controller medication and either with or without oral corticosteroids (OCS) and have experienced two or more exacerbations in the preceding 12 months. Additional inclusion criteria included current nonsmoker and a prebronchodilator FEV1 of <80 percent predicted normal (<90 percent for adolescents aged 12 to 17). Individuals were randomized in a 1:1 ratio to treatment with tezepelumab-ekko (Tezspire) 210 mg SC every four weeks or placebo. Baseline asthma medications were maintained throughout the study. The primary endpoint was the annualized rate of asthma exacerbations at one year. One of the secondary endpoints included changes in FEV1 values. Of the 1061 individuals, 529 were assigned to receive tezepelumab-ekko (Tezspire) and 532 were assigned to receive the placebo. The primary endpoint of annualized rate of asthma exacerbations was 0.93 (95 percent CI, 0.80 to 1.07) in the tezepelumab-ekko (Tezspire) group and 2.10 (95 percent CI, 1.84 to 2.39) in the placebo group (rate ratio, 0.44; 95 percent CI, 0.37 to 0.53; p<0.001). There were significant reductions in the asthma exacerbation rates regardless of the baseline eosinophil or other biomarker levels. The secondary endpoint of change in FEV1 values was 0.23 liters in the tezepelumab-ekko (Tezspire) group and 0.09 liters in the placebo group (difference, 0.13 liters; 95 percent CI, 0.08 to 0.18; p<0.001). The treatment effect on this value was seen as early as two weeks and were sustained throughout the remainder of the clinical trial. There were decreases in the eosinophil and FeNO levels in the tezepelumab-ekko (Tezspire) treatment group starting as early as two weeks and sustained throughout the trial year.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

American Hospital Formulary Service (AHFS). Tezepelumab-ekko (Tezspire®). AHFS Drug Information 2023. [LexiComp Web site]. 04/21/2023. Available at: https://online.lexi.com/lco/action/home [via subscription only]. Accessed November 1, 2023.

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US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Tezepelumab-ekko (Tezspire®). Prescribing information. [FDA Web site]. 05/26/2023. Available at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed November 1, 2023.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J82.83	Eosinophilic asthma

HCPCS Level II Code Number(s)

J2356	Injection, tezepelumab-ekko, 1 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.144b:

03/28/2025	This policy has been reissued in accordance with the Company's annual review process.
05/07/2024	This policy has been reissued in accordance with the Company's annual review process.
01/02/2024	This version of the policy will become effective 01/02/2024. This policy was reviewed. The intent of the policy remains unchanged. The references were updated accordingly.

Revisions from MA08.144a

07/01/2022	This version of the policy will become effective 07/01/2022. Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following HCPCS codes have been **deleted** from this policy: J3590 Unclassified biologics C9399 Unclassified drugs or biologicals The following HCPCS code has been **added** to this policy: J2356 Injection, tezepelumab-ekko, 1 mg

MA08.144:

04/11/2022	The following new policy has been developed to communicate the Company's coverage criteria for tezepelumab-ekko (Tezspire) in accordance with the US Food and Drug Administration (12/17/2021).

Version Effective Date:
07/01/2022
Version Issued Date:
07/01/2022
Version Reissued Date:
03/28/2025