

Medical Policy Bulletin

Title:

Tezepelumab-ekko (Tezspire®)

Policy #:

MA08.144c

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.

SEVERE ASTHMA

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]):
 - Prebronchodilator 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 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

CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS

Initial Therapy

Tezepelumab-ekko (Tezspire), administered by 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 inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP) for at least 12 months with ALL of the following:

- Severity consistent with need for surgery as defined by total nasal polyp score (NPS) of 5 or more (2 or more for each nostril)
- Nasal congestion score (NCS) of 2 or more
- Ongoing documented nasal polyposis (NP) symptoms of greater than 8 weeks (e.g., rhinorrhea, reduction/loss of smell)
- Treatment with at least ONE of the following:
 - Continuation of treatment with intranasal corticosteroids (INCS)
 - **Any history of nasal polyp surgery (or contraindications/intolerance to)**

Continuation Therapy

Tezepelumab-ekko (Tezspire), administered by SC injection by a healthcare professional provider, is considered medically necessary and, therefore, covered for continuation therapy for the add-on treatment of CRSwNP when there is documentation confirming ANY of the following:

- Clinical improvement in NPS
- Improvement in NCS
- Improvement in NP symptoms

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

There is no Medicare coverage determination addressing tezepelumab-ekko (Tezspire); therefore, the Company policy is applicable.

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.

NASAL POLYP SCORE

The nasal polyp score (NPS) is based on the sum of the scores from both nostrils. The scores should be obtained by evaluating the nostrils with a nasal endoscopy.

Score	Polyp size
0	No polyp
1	Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate
2	Polyps reaching below the lower border of the middle turbinate
3	Polyps reaching the lower border of the inferior turbinate or a middle meatal polyp with a score of 2 with any additional polyp medial to the middle turbinate
4	Large polyps causing complete or near complete obstruction of the inferior nasal cavity, i.e., touching the floor of the nose

ClinicalTrials.gov. Efficacy and safety of tezepelumab in participants with severe chronic rhinosinusitis with nasal polyposis (WAYPOINT). ClinicalTrials.gov Identifier: NCT04851964. First Posted: April 21, 2021. Last Update Posted: January 27, 2026. Available at: <https://clinicaltrials.gov/>.

NASAL CONGESTION SCORE

The nasal congestion score (NCS) is based on the individual rating the severity of their worst nasal congestion over the previous 24 hours.

Score	Congestion severity
0	None
1	Mild
2	Moderate
3	Severe

ClinicalTrials.gov. Efficacy and safety of tezepelumab in participants with severe chronic rhinosinusitis with nasal polyposis (WAYPOINT). ClinicalTrials.gov Identifier: NCT04851964. First Posted: April 21, 2021. Last Update Posted: January 27, 2026. Available at: <https://clinicaltrials.gov/>.

US FOOD AND DRUG ADMINISTRATION STATUS

Tezepelumab-ekko (Tezspire) was approved by the US Food and Drug Administration (FDA) on December 17, 2021, for the add-on maintenance treatment of adult and pediatric individuals aged 12 years and older with severe asthma. Supplemental approvals for tezepelumab-ekko (Tezspire) have since been issued by the FDA.

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 and chronic rhinosinusitis with nasal polyposis.

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)

Tezepelumab-ekko (Tezspire) is a human monoclonal antibody designed to reduce inflammation associated with chronic rhinosinusitis with nasal polyps and severe asthma by targeting an early driver of the inflammatory process. It works by binding to thymic stromal lymphopoietin (TSLP), which is a signaling protein, known as a cytokine, released primarily by epithelial cells that line the airways and nasal passages. TSLP plays an upstream role in inflammation by activating multiple immune cells, including eosinophils, mast cells, macrophages, lymphocytes, and group 2 innate lymphoid cells, which then produce additional inflammatory mediators such as interleukins and immunoglobulin E (IgE). By blocking TSLP from interacting with its receptor, tezepelumab-ekko interrupts several inflammatory pathways at once rather than targeting a single downstream biomarker.

According to the US Food and Drug Administration (FDA) label, the recommended dosage of tezepelumab-ekko (Tezspire) by subcutaneous (SC) injection is 210 mg once every 4 weeks. Tezepelumab-ekko (Tezspire) vial and prefilled syringe are intended for administration by a healthcare provider. The prefilled pen can be administered by either the individual or caregiver (after proper training in injection technique) or a healthcare provider.

PEER-REVIEWED LITERATURE

SEVERE ASTHMA

Tezepelumab-ekko (Tezspire) was studied in a multicenter, phase 2, randomized, placebo-controlled, parallel-group, double-blind, dose-ranging clinical trial in adult individuals with inadequately controlled, severe asthma (Corren et al., 2017; NCT02054130; PATHWAY). Eligibility criteria included current nonsmoker for 6 months or more, poorly controlled asthma despite treatment with a long-acting beta agonist (LABA) and either medium (250 to 500 µg/d of inhaled fluticasone [or equivalent]) or high (>500 µg/d of fluticasone [or equivalent]) for at least 6 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 4 weeks, 210 mg every 4 weeks, 280 mg every 2 weeks) of tezepelumab-ekko (Tezspire) SC or placebo. Baseline asthma treatment medications were maintained throughout the study. The primary endpoint was the annualized rate of asthma exacerbations at 1 year. One of the secondary endpoints included changes in FEV₁ values. Of the 550 individuals randomly assigned equally into the four groups, the annualized rates of asthma exacerbations at 1 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], 42–75; $P<0.001$), 71 percent (90 percent CI, 54–82; $P<0.001$), and 66 percent (90 percent CI, 47–79; $P<0.001$) 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, 0.02–0.22; $P=0.015$), 0.13 liters (95 percent CI, 0.03–0.23; $P=0.009$), and 0.15 liters (95 percent CI, 0.05–0.25; $P=0.002$) in the low-dose, medium-dose, and high-dose groups, respectively. The treatment effects on these values were seen as early as 4 weeks and were sustained for the remainder of the clinical trial. There were also substantial and continued decreases in the eosinophil and fractional exhaled nitric oxide (FeNO) levels in all the tezepelumab-ekko (Tezspire) treatment groups as early as 4 weeks.

Tezepelumab-ekko (Tezspire) was studied in a multicenter, phase 3, randomized, placebo-controlled, parallel group, double-blind clinical trial in adult and adolescent individuals with severe, uncontrolled asthma (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 3 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 less than 80 percent predicted normal (<90 percent for adolescents aged 12 to 17). Individuals were randomly assigned in a 1:1 ratio to treatment with tezepelumab-ekko (Tezspire) 210 mg SC every 4 weeks or placebo. Baseline asthma medications were maintained throughout the study. The primary endpoint was the annualized rate of asthma exacerbations at 1 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, 0.80–1.07) in the tezepelumab-ekko (Tezspire) group and 2.10 (95 percent CI, 1.84–2.39) in the placebo group (rate ratio, 0.44; 95 percent CI, 0.37–0.53; $P<0.001$). 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, 0.08–0.18; $P<0.001$). The treatment effect on this value was seen as early as 2 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 2 weeks and sustained throughout the trial year.

CHRONIC RHINOSINUSITIS WITH NASAL POLYPOSIS

Tezepelumab-ekko (Tezspire) was studied in a multicenter, phase 3, randomized, placebo-controlled, parallel group, double-blind clinical trial in individuals with chronic rhinosinusitis with nasal polyposis (CRSwNP) (Lipworth et al, 2025; NCT04851964; WAYPOINT). A total of 408 participants were enrolled and randomly assigned in a 1:1 ratio into two cohorts, consisting of 203 participants receiving tezepelumab-ekko (Tezspire) and 205 participants receiving placebo, both added to standard of care intranasal corticosteroid therapy. Treatment was administered subcutaneously every 4 weeks for 52 weeks. The co-primary endpoints were the change from baseline at week 52 in total nasal polyp score (NPS), assessed by nasal endoscopy, and the change from baseline at week 52 in biweekly mean nasal congestion score (NCS), assessed using a daily symptom diary. Key secondary endpoints included time to nasal polyp surgery decision and/or systemic corticosteroid use, change from baseline in loss of smell score, change from baseline in Sino-Nasal Outcome Test-22 (SNOT-22) total score, change from baseline in Lund-Mackay sinus computed tomography (CT) score, and change from baseline in total symptom score. NPS is a measure of nasal polyp size scored from 0 to 8. NCS reflects nasal congestion severity on a 0 to 3 scale. SNOT-22 is a validated 22-item questionnaire assessing sino-nasal quality of life, with higher scores indicating greater disease burden.

At week 52, tezepelumab-ekko (Tezspire) demonstrated statistically significant improvements compared with placebo across both co-primary endpoints. The least-squares mean difference versus placebo for change in total NPS was -2.07 (95 percent CI, -2.39 to -1.74; $P < 0.001$). The least-squares mean difference for change in biweekly mean NCS was -1.03 (95 percent CI, -1.20 to -0.86; $P < 0.001$). Significant improvements were also observed for all key secondary endpoints. The loss of smell score improved with a least-squares mean difference of -1.00 (95 percent CI, -1.18 to -0.83; $P < 0.001$). The SNOT-22 total score improved by -27.26 points (95 percent CI, -32.32 to -22.21; $P < 0.001$) compared with placebo. Tezepelumab-ekko (Tezspire) reduced the risk of requiring nasal polyp surgery and/or systemic corticosteroid treatment by 92 percent relative to placebo (hazard ratio [HR], 0.08; 95 percent CI, 0.03 to 0.17; $P < 0.001$), with a 98 percent reduction in nasal polyp surgery alone and an 88 percent reduction in systemic corticosteroid use. The Lund-Mackay score, which quantifies sinus opacification on CT scans from 0 to 24, improved with a least-squares mean difference of -5.72 (95 percent CI, -6.39 to -5.06; $P < 0.001$). The percentage of on-treatment adverse events were approximately equal in the two cohorts. Overall, the frequency of adverse events was higher in the placebo cohort as compared to the tezepelumab-ekko (Tezspire) cohort.

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. [UpToDate Lexidrug Web site]. 03/24/2026. Available at: <https://online.lexi.com/lco/action/home> [via subscription only]. Accessed March 26, 2026.

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UpToDate® Lexidrug™. Tezepelumab-ekko (Tezspire®). [UpToDate Lexidrug Web site]. 02/16/2026. Available at: <https://online.lexi.com/lco/action/home> [via subscription only]. Accessed March 26, 2026.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Tezepelumab-ekko (Tezspire®). Prescribing information. [FDA Web site]. 10/17/2025. Available at: <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>. Accessed March 26, 2026.

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

TEZEPELUMAB-EKKO (TEZSPIRE) IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING INDICATION:

For chronic rhinosinusitis with nasal polyposis, multiple diagnoses are required:

J32.0 Chronic maxillary sinusitis
J32.1 Chronic frontal sinusitis
J32.2 Chronic ethmoidal sinusitis
J32.3 Chronic sphenoidal sinusitis

J32.4 Chronic pansinusitis
J32.8 Other chronic sinusitis
J32.9 Chronic sinusitis, unspecified

AND at least one of the following:

J33.0 Polyp of nasal cavity
J33.1 Polypoid sinus degeneration
J33.8 Other polyp of sinus
J33.9 Nasal polyp, unspecified

HCPCS Level II Code Number(s)

J2356 Injection, tezepelumab-ekko, 1 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.144c:

09/18/2026	This version of the policy will become effective 09/18/2026. The following indication with criteria has been added to this policy as medically necessary: chronic rhinosinusitis with nasal polyposis The following ICD-10 codes have been added to this policy: • J32.0 Chronic maxillary sinusitis • J32.1 Chronic frontal sinusitis • J32.2 Chronic ethmoidal sinusitis • J32.3 Chronic sphenoidal sinusitis • J32.4 Chronic pansinusitis • J32.8 Other chronic sinusitis • J32.9 Chronic sinusitis, unspecified • J33.0 Polyp of nasal cavity • J33.1 Polypoid sinus degeneration • J33.8 Other polyp of sinus • J33.9 Nasal polyp, unspecified
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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.
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	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
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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).
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Version Effective Date:

09/18/2026

Version Issued Date:

09/18/2026

Version Reissued Date:

N/A