

Tezepelumab-ekko (TEZSPIRE) Injection

National Drug Monograph

June 2022

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA Approval Information

Description/Mechanism of Action

- Tezepelumab is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody (IgG2λ)

Indication(s) Under Review in This Document

- Indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma

Dosage Form(s) Under Review

- 210 mg/1.91 mL (110 mg/mL) solution available in a single-dose glass vial and in a prefilled-syringe
- Recommended dosage is 210 mg administered once every 4 weeks administered by subcutaneous injection.
- Intended for administration by a healthcare provider

Clinical Evidence Summary

Efficacy Considerations

Two 52-week trials, PATHWAY and NAVIGATOR, compared tezepelumab 210mg every 4 weeks to placebo in patients with severe, uncontrolled asthma receiving medium-high dose inhaled corticosteroids and one additional controller medication. Both trials required a history of exacerbations in the prior year (Table 1). The PATHWAY trial also included 2 treatment doses that are not marketed, and the results have been excluded from this review.

Patient demographics include mean age 50-52 years, 64-66% female, 62-92% white, never smoked 80%, mean duration of asthma 17-22 years. Other baseline patient details are shown in table 1.

The primary outcome was the annualized rate of asthma exacerbations over a period of 52 weeks. Secondary endpoints included FEV1, Asthma Control Questionnaire-6 score, and Asthma Quality of Life Questionnaire score.

Tezepelumab reduced exacerbations and improved lung function, asthma control, and health-related quality of life compared to placebo. Higher baseline blood eosinophil counts were associated with greater reduction in exacerbations (Table 1).

Reduction in exacerbations was also noted regardless of perennial allergy status (Table 1). In a post-hoc analysis of the PATHWAY trial according to eligibility for omalizumab per US labeling, asthma exacerbations were reduced by 82% for those who were eligible for omalizumab and by 63% for those who were not eligible for omalizumab compared to placebo.

Table 1: Efficacy results from clinical trials

Study	Design	Baseline	Select Results																																								
PATHWAY Phase 2 N=275 52 weeks TEZ 210 Q4W vs. PBO	Med-high dose ICS + LABA ≥2 exacerbations req systemic steroids or ≥ 1 resulting in hospitalization in previous 12 mos.	<ul style="list-style-type: none"> Med-dose ICS 52%; high-dose ICS 48%; OCS 9% Pre-BD FEV1 1.853 (59.5% predicted) Blood EOS 372 cells/μL (56% ≥ 250) Serum total IgE 479 IU/mL ACQ-6 score 2.68 AQLQ(S)+12 overall score 4.1 FENO 34.5ppb (46% ≥ 24ppb) Mean number exacerbations 2.4 1- 2 exacerbations 78%; ≥3 exacerbations 22% FEIA positive to perennial aeroallergen 57% 	Annualized Asthma Exacerbation Rate <table border="1"> <thead> <tr> <th></th> <th>TEZ</th> <th>PBO</th> <th>Rate Ratio (95%CI)</th> </tr> </thead> <tbody> <tr> <td>Overall</td> <td>0.20</td> <td>0.72</td> <td>0.29 (0.16, 0.51)*</td> </tr> <tr> <td>Hosp/ER visit</td> <td>0.03</td> <td>0.18</td> <td>0.15 (0.04, 0.58)</td> </tr> <tr> <td>Hosp</td> <td>0.02</td> <td>0.14</td> <td>0.14 (0.03, 0.71)</td> </tr> <tr> <td colspan="4">Reduction vs PBO</td> </tr> <tr> <td>EOS ≥250</td> <td>0.26</td> <td>0.78</td> <td>65% (27%, 83%)*</td> </tr> <tr> <td>EOS <250</td> <td>0.14</td> <td>0.65</td> <td>79% (48%, 92%)*</td> </tr> <tr> <td>Allergic</td> <td>0.14</td> <td>0.75</td> <td>82% (56%, 93%)*</td> </tr> <tr> <td>Non-allergic</td> <td>0.26</td> <td>0.65</td> <td>54% (-1%, 79%)</td> </tr> </tbody> </table>		TEZ	PBO	Rate Ratio (95%CI)	Overall	0.20	0.72	0.29 (0.16, 0.51)*	Hosp/ER visit	0.03	0.18	0.15 (0.04, 0.58)	Hosp	0.02	0.14	0.14 (0.03, 0.71)	Reduction vs PBO				EOS ≥250	0.26	0.78	65% (27%, 83%)*	EOS <250	0.14	0.65	79% (48%, 92%)*	Allergic	0.14	0.75	82% (56%, 93%)*	Non-allergic	0.26	0.65	54% (-1%, 79%)				
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Abbreviations: ACQ-6 =Asthma Control Questionnaire-6; AQLQ(S)= Asthma Quality of Life Questionnaire; EOS=eosinophils; FEIA=fluorescence enzyme immunoassay; FENO=fraction of exhaled nitric oxide; ICS=inhaled corticosteroid; OCS=oral corticosteroid; PBO=placebo; Pre-BD=prebronchodilator; TEZ=tezepelumab

^ACQ-6 range 0 (no impairment) to 6 (maximum impairment). The minimum clinically important difference is 0.5 points.

‡AQLQ(S)+12 range 1(maximum impairment) to 7 (no impairment). The minimum clinically important difference is 0.5 points.

*Statistically significant difference vs placebo where p-values were calculated (p-values not calculated for all outcomes)

Safety Considerations

- **Boxed warnings:** None
- **Contraindications:** contraindicated in patients who have known hypersensitivity to tezepelumab or any of its excipients
- **Other warnings / precautions:**
 - Hypersensitivity Reactions: Hypersensitivity reactions (e.g., rash, allergic conjunctivitis) can occur after administration of tezepelumab. Initiate appropriate treatment as clinically indicated in the event of a hypersensitivity reaction.

- Risk Associated with Abrupt Reduction in Corticosteroid Dosage: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with tezepelumab. Decrease corticosteroids gradually, if appropriate.
 - Parasitic (Helminth) Infection: Treat patients with pre-existing helminth infections before therapy with tezepelumab. If patients become infected while receiving tezepelumab and do not respond to anti-helminth treatment, discontinue tezepelumab until the parasitic infection resolves.
 - Vaccination: Concomitant use of tezepelumab and live attenuated vaccines has not been evaluated. Avoid use of live attenuated vaccines.
- **Adverse reactions (tezepelumab vs placebo)**
 - **Common** Most common adverse reactions (incidence \geq 3%) are pharyngitis (4% vs 3%), arthralgia (4% vs 3%), and back pain (4% vs 3%)
 - **Serious Adverse events:** 9.5% vs 13% (PATHWAY)/ 9.8% vs 13.7% (NAVIGATOR)
 - **Deaths:** None
 - **Discontinuation:** 1.5% vs 0.7% (PATHWAY)/ 2.1% vs 3.6% (NAVIGATOR)
 - **Adverse events of special interest**
 - Injection site reactions (e.g., injection site erythema, injection site swelling, injection site pain) occurred at a rate of 3.3% vs 2.7% in patients treated with tezepelumab and placebo respectively.
 - Anti-drug antibodies (ADA) were detected at any time in 29/601 (5%) patients who received tezepelumab 210mg every 4 weeks during the 48 to 52-week study period. Of these 29 patients, 11 patients (2%) developed treatment-emergent antibodies and 1 patient (<1%) developed neutralizing antibodies. ADA titers were generally low and transient. No evidence that ADA had an impact on pharmacokinetics, pharmacodynamics, efficacy, or safety was observed.

Other Considerations

According to a review by the Institute for Clinical and Economic Review (ICER), tezepelumab would need to be priced at between \$9,000 and \$12,000 annually to meet standard thresholds for cost-effectiveness. At present, the biologic agents used to treat asthma exceed this price threshold.

Other Therapeutic Options

Alternative biologic treatments for asthma are listed in table 3.

Table 3 Treatment Alternatives (Biologic agents used in asthma)

Drug	Formulary status	Other Considerations
Tezepelumab	TBD	<ul style="list-style-type: none"> Severe asthma Dosed Q4W Intended for administration by a healthcare provider Available in vial and PFS Did not demonstrate a statistically significant reduction in maintenance OCS compared to placebo
Benralizumab	PA-F	<ul style="list-style-type: none"> Severe asthma with eosinophilic phenotype Dosed Q8W (after initial dose of Q4W x3 doses) May be self-administered Available in auto-injector and PFS Data showing reduction in maintenance OCS dose
Mepolizumab	NF	<ul style="list-style-type: none"> Severe asthma with eosinophilic phenotype Dosed Q4W May be self-administered Available in auto-injector and PFS Data showing reduction in maintenance OCS dose
Dupilumab	NF	<ul style="list-style-type: none"> Moderate-severe asthma with eosinophilic phenotype or oral steroid dependent asthma 200mg or 300mg Q2W (after initial dose of 400mg or 600mg) May be self-administered Available in PFS and pen
Omalizumab	PA-F	<ul style="list-style-type: none"> Moderate-severe asthma with positive skin test or in vitro reactivity to a perennial aeroallergen 75 to 375mg Q2-4W depending on pretreatment IgE level and body weight Therapy initiated in healthcare setting; may be self-administered for select patients Available in vial and PFS

ICS=inhaled corticosteroid; LABA=long-acting beta-agonist; NF=nonformulary; OCS=oral corticosteroid; PA-F= formulary with prior authorization; PFS=prefilled syringe

Projected Place in Therapy

Tezepelumab can be used in patients with severe asthma without regards to eosinophilic phenotype or biomarker limitations. In the Phase 3 NAVIGATOR trial, the risk of asthma exacerbations was reduced by 54% with modest improvement in FEV1, symptoms, and quality of life relative to placebo. In a dedicated oral corticosteroid reduction trial, tezepelumab did not demonstrate a statistically significant reduction in maintenance oral corticosteroids, without loss of asthma control, compared to placebo. Tezepelumab is intended for administration by a healthcare provider.

Projected place in therapy includes use in patients with severe asthma without an eosinophilic phenotype (i.e., blood eosinophil count less than 150 cells/ μ L) who are receiving optimal therapy (inhaled corticosteroid and long-acting beta-agonist and/or long-acting anticholinergic) and who have inadequate symptom control or asthma exacerbations. It may also be used in patients who have had an inadequate response or adverse events to other biologics used for asthma (i.e., benralizumab, mepolizumab, dupilumab, omalizumab).

References

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Corren J, Ambrose CS, Sařapa K, Roseti SL, et al. [Efficacy of Tezepelumab in Patients with Severe, Uncontrolled Asthma and Perennial Allergy](#). Allergy Clin Immunol Pract. 2021 Dec;9(12):4334-4342.

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Wechsler M, Gow AM, Brightling CE, et al. Oral Corticosteroid-Sparing Effect of Tezepelumab in Adults with Severe Asthma. American Thoracic Society. 2021;203:A1197.

Prepared May 2022. Contact person: Deb Khachikian, PharmD, National PBM Clinical Pharmacy Program Manager, Formulary management, VA Pharmacy Benefits Management Services (12PBM)
