Department of Health and Human Services
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	March 24, 2025
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Product Name:	Tezspire (tezepelumab-ekko) injection
Pediatric Labeling Approval Date:	December 17, 2021
Application Type/Number:	BLA 761224
Applicant:	AstraZeneca AB
TTT Record ID:	2025-13217

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Tezspire (tezepelumab-ekko) injection in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with tezepelumab in pediatric patients.

Tezspire (tezepelumab-ekko) injection is a thymic stromal lymphopoietin blocker and human monoclonal antibody that was initially approved in the U.S. on December 17, 2021. Tezspire is currently indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. Tezspire is not indicated for relief of acute bronchospasm or status asthmaticus.

This pediatric postmarketing safety review was prompted by pediatric labeling at initial approval on December 12, 2021, that included an indication for pediatric use in patients aged 12 years and older.

DPV has not previously performed a pediatric postmarketing pharmacovigilance review for tezepelumab for the Pediatric Advisory Committee.

DPV reviewed all U.S. serious FAERS reports with tezepelumab in pediatric patients less than 18 years of age from December 17, 2021 – February 9, 2025, and identified six reports; however, all reports were excluded from further discussion.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with tezepelumab in pediatric patients less than 18 years of age.

DPV did not identify any new pediatric safety concerns for tezepelumab at this time and will continue routine pharmacovigilance monitoring for tezepelumab.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Tezspire (tezepelumab-ekko) injection in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with tezepelumab in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Tezspire (tezepelumab-ekko) injection is a thymic stromal lymphopoietin blocker and human monoclonal antibody that was initially approved in the U.S. on December 17, 2021.[1] Tezspire is currently indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. Tezspire is not indicated for relief of acute bronchospasm or status asthmaticus.[2]

This pediatric postmarketing safety review was prompted by pediatric labeling at initial approval on December 12, 2021, that included an indication for pediatric use in patients aged 12 years and older.

DPV has not previously performed a pediatric postmarketing pharmacovigilance review for tezepelumab for the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Tezspire (tezepelumab-ekko) injection labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional Tezspire labeling information, please refer to the full prescribing information.[2]

----------CONTRAINDICATIONS----------
Known hypersensitivity to tezepelumab-ekko or excipients. (4)

----------WARNINGS AND PRECAUTIONS----------
- Hypersensitivity Reactions: Hypersensitivity reactions have been observed in the clinical trials (e.g., rash, allergic conjunctivitis) following the administration of TEZSPIRE. Postmarketing cases of anaphylaxis have been reported. Initiate appropriate treatment as clinically indicated in the event of a hypersensitivity reaction. (5.1)
- Risk Associated with Abrupt Reduction in Corticosteroid Dosage: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with TEZSPIRE. Decrease corticosteroids gradually, if appropriate. (5.3)
- Parasitic (Helminth) Infection: Treat patients with pre-existing helminth infections before therapy with TEZSPIRE. If patients become infected while receiving TEZSPIRE and do not respond to antihelminth treatment, discontinue TEZSPIRE until the parasitic infection resolves. (5.4)
- Vaccination: Avoid use of live attenuated vaccines. (5.5)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence ≥ 3%) are pharyngitis, arthralgia, and back pain. (6.1)

8.4 Pediatric Use
The safety and effectiveness of TEZSPIRE for the add-on maintenance treatment of severe asthma have been established in pediatric patients aged 12 years and older [see Adverse Reactions (6.1) and Clinical Studies (14)]. Use of TEZSPIRE for this indication is supported by evidence from a total of 82 pediatric patients aged 12 to 17 years enrolled in NAVIGATOR and received treatment with TEZSPIRE 210 mg subcutaneously every 4 weeks (n=41) or placebo (n=41). Compared with placebo, improvements in

annualized asthma exacerbation (rate ratio 0.70; 95% CI 0.34, 1.46) and FEV1 (LS mean change versus placebo 0.17 L; 95% CI -0.01, 0.35) were observed in pediatric patients treated with TEZSPIRE. The safety profile and pharmacodynamic responses in pediatric patients were generally similar to the overall study population.

The safety and effectiveness in patients younger than 12 years of age have not been established.

2 METHODS AND MATERIALS

2.1 FAERS SEARCH STRATEGY

DPV searched the FAERS database with the strategy described in **Table 1**.

Table 1. FAERS Search Strategy*	
Date of search	February 10, 2025
Time period of search	December 17, 2021† - February 9, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: Tezepelumab, tezepelumab-ekko
MedDRA search terms (Version 27.1)	All Preferred Terms
Other search terms‡	Case Seriousness: Serious Country Derived: USA

* See Appendix A for a description of the FAERS database.
† Tezspire U.S. approval date
‡ For the purposes of this review, the following outcomes qualify as serious: death, life-threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.
Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities; USA=United States of America

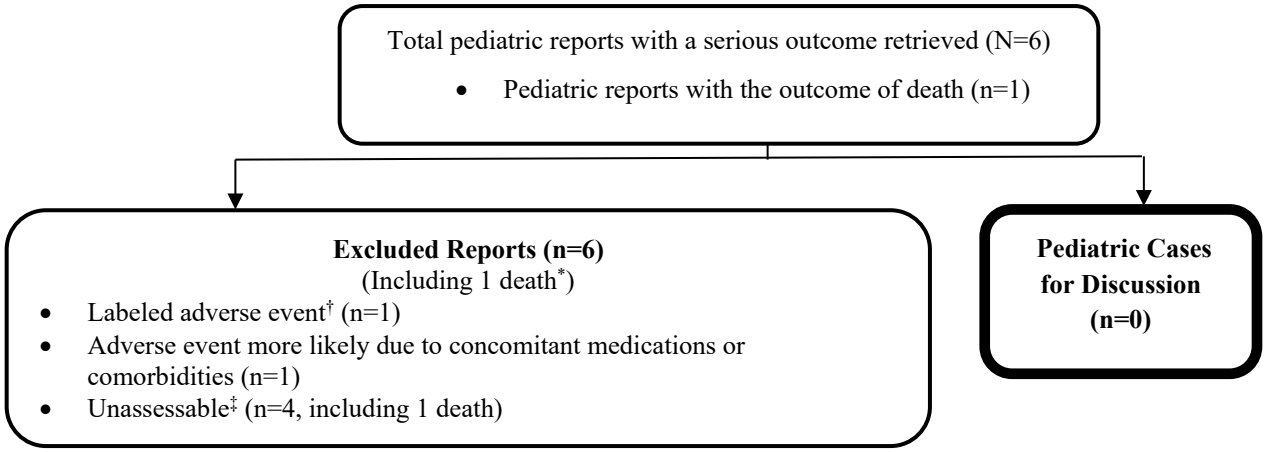
3 RESULTS

3.1 FAERS

3.1.1 Selection of U.S. Serious Pediatric Cases in FAERS

Our FAERS search retrieved six U.S. serious pediatric reports for patients less than 18 years old from December 17, 2021 – February 9, 2025. We reviewed all U.S. FAERS pediatric reports with a serious outcome. We excluded all six reports from the case series for the reasons listed in **Figure 1**. **Figure 1** presents the selection of cases for the pediatric case series.

Figure 1. Selection of U.S. Serious Pediatric Cases With Tezepelumab



* One excluded U.S. FAERS report described a fatal outcome. The case contained no information to understand clinical context or perform a causality assessment with tezepelumab.
† Labeled adverse event does not represent increased severity.
‡ Unassessable: The report cannot be assessed for causality because there is insufficient information reported (i.e., unknown time to event, concomitant medications and comorbidities, clinical course and outcome), the information is contradictory, or information provided in the report cannot be supplemented or verified.

3.1.2 Summary of U.S. Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.3 Summary of U.S. Serious Non-Fatal Pediatric Cases (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all U.S. serious FAERS reports with tezepelumab in pediatric patients less than 18 years of age from December 17, 2021 – February 9, 2025, and identified six reports; however, all reports were excluded from further discussion.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with tezepelumab in pediatric patients less than 18 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for tezepelumab at this time and will continue routine pharmacovigilance monitoring for tezepelumab.

6 REFERENCES

1. Tezspire (tezepelumab-ekko) injection. [Prescribing information]. Thousand Oaks, CA; AstraZeneca AB: December 2021.
2. Tezspire (tezepelumab-ekko) injection. [Prescribing information]. Thousand Oaks, CA; AstraZeneca AB: May 2023.

7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.