Department of Health and Human Services
Public Health Service
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:	October 24, 2023
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Product Name:	Taltz (ixekizumab) injection
Pediatric Labeling Approval Date:	March 26, 2020
Application Type/Number:	BLA 125521
Applicant:	Eli Lilly and Co.
TTT Record ID:	2023-5805

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Taltz (ixekizumab) 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 serious unlabeled adverse events associated with ixekizumab in pediatric patients.

Taltz (ixekizumab) injection is a humanized interleukin-17A antagonist that was initially approved in the U.S. on March 22, 2016. Ixekizumab is currently indicated for the following:

- Patients aged 6 years and older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy
- Adults with active psoriatic arthritis
- Adults with active ankylosing spondylitis
- Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation

This pediatric postmarketing safety review was prompted by pediatric labeling on March 26, 2020, which expanded the indication of ixekizumab for use in pediatric patients aged 6 years and older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. A pediatric safety review for ixekizumab has not been previously presented to the Pediatric Advisory Committee.

DPV searched FAERS for all serious reports with ixekizumab in pediatric patients less than 18 years of age from March 22, 2016 – July 30, 2023, and identified eight reports. However, all reports were excluded from further discussion.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Taltz (ixekizumab) 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 serious unlabeled adverse events associated with ixekizumab in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY[1]

Taltz (ixekizumab) injection is a humanized interleukin-17A antagonist that was initially approved in the U.S. on March 22, 2016. Ixekizumab is currently indicated for the following:

- Patients aged 6 years and older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy
- Adults with active psoriatic arthritis
- Adults with active ankylosing spondylitis
- Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation

This pediatric postmarketing safety review was prompted by pediatric labeling on March 26, 2020, which expanded the indication of ixekizumab for use in pediatric patients aged 6 years and older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Support for the use of ixekizumab in pediatric patients aged 6 years and older derived from a placebo-controlled trial in 171 pediatric subjects 6 – <18 years old with moderate-to-severe plaque psoriasis (NCT03073200). Overall, the safety profile observed in pediatric subjects with plaque psoriasis treated with ixekizumab every 4 weeks was consistent with the safety profile in adult subjects with plaque psoriasis with the exception of the frequencies of conjunctivitis (2.6%), influenza (1.7%), and urticaria (1.7%). Crohn's disease occurred at a greater frequency in the treatment group (0.9%, n=4 patients) compared with placebo group (0%) during the 12-week placebo-controlled period. The safety and effectiveness of ixekizumab has not been established in patients less than 6 years old.

A pediatric safety review for ixekizumab has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Taltz labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional Taltz labeling information, please refer to the full prescribing information.[1]

---------- CONTRAINDICATIONS ----------
Serious hypersensitivity reaction to ixekizumab or to any of the excipients. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Infections: Serious infections have occurred. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops, discontinue TALTZ until the infection resolves. (5.1)

- Tuberculosis (TB): Evaluate for TB prior to initiating treatment. (5.2)
- Hypersensitivity: If a serious allergic reaction occurs, discontinue TALTZ immediately and initiate appropriate therapy. (5.3)
- Inflammatory Bowel Disease: Crohn's disease and ulcerative colitis, including exacerbations, occurred during clinical trials. Monitor closely when prescribing TALTZ to patients with inflammatory bowel disease (IBD). Discontinue TALTZ and initiate appropriate medical management if IBD develops. (5.4)
- Immunizations: Avoid use of live vaccines. (5.5)

---------- ADVERSE REACTIONS ----------

8.4 Pediatric Use
The safety and effectiveness of TALTZ have been established in pediatric subjects aged 6 years to less than 18 years with moderate-to-severe plaque psoriasis. The safety and effectiveness of TALTZ in other pediatric indications and for pediatric subjects less than 6 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	July 31, 2023
Time period of search	March 22, 2016† - July 30, 2023
Search type	RxLogix Post-Market Cases
Product terms	Product Active Ingredient: Ixekizumab
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Taltz U.S. approval date Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities	

3 RESULTS

3.1 FAERS

3.1.1 Total Number of FAERS Reports by Age

Table 2 presents the number of adult and pediatric FAERS reports from March 22, 2016 – July 30, 2023, with ixekizumab.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From March 22, 2016 – July 30, 2023, With Ixekizumab			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 18 years)	12,009 (10,486)	2,647 (1,144)	216 (125)
Pediatrics (0 - < 18 years)	142 (138)‡	8 (4)‡	1 (1)‡

* May include duplicates and transplacental exposures, and have not been assessed for causality

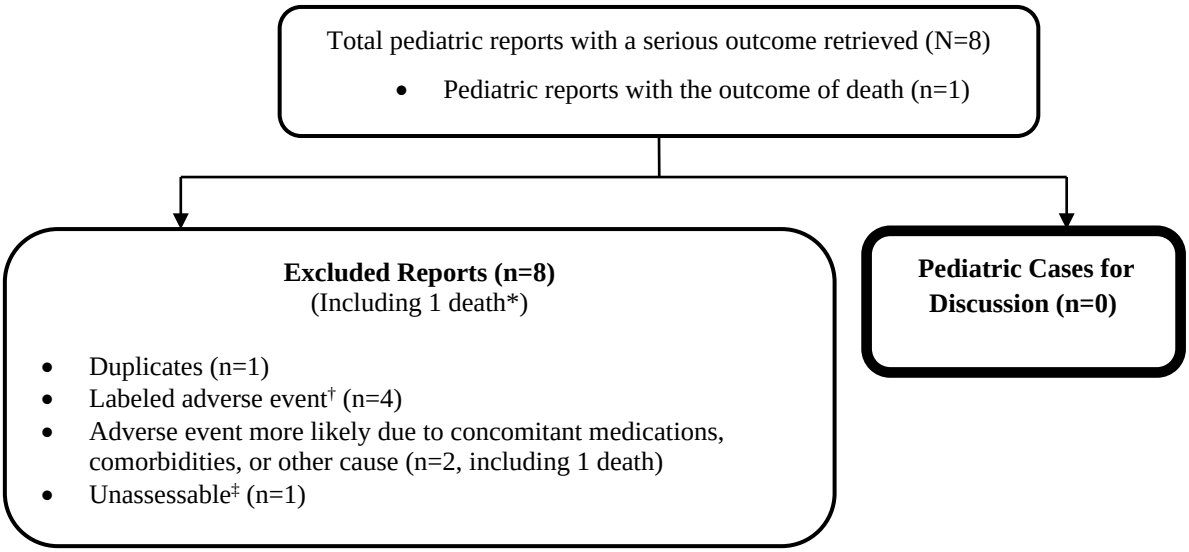
† For the purposes of this review, the following outcomes qualify as serious: death, life- threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.

‡ See Figure 1. One additional report of pediatric death was identified among reports not reporting an age. This report is reflected in the counts of pediatric reports.

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved eight serious pediatric reports from March 22, 2016 – July 30, 2023. We reviewed all FAERS pediatric reports with a serious outcome. We excluded all eight 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 Serious Pediatric Cases With Ixekizumab



* One excluded FAERS report described a fatal outcome. The death was not determined to be attributed to ixekizumab. The report described a patient who died in a motor vehicle accident.

† Labeled adverse event does not represent increased severity or frequency.

‡ 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.

3.1.3 Summary of Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.4 Summary of Serious Non-Fatal Pediatric Cases (N=0)

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

4 DISCUSSION

DPV searched FAERS for all serious reports with ixekizumab in pediatric patients less than 18 years of age from March 22, 2016 – July 30, 2023, and identified eight reports. However, all reports were excluded from further discussion.

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

5 CONCLUSION

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

6 REFERENCES

1. Taltz (ixekizumab) injection, for subcutaneous use [Prescribing information]. Indianapolis, IN; Eli Lilly and Company: July, 2022.

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.

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