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:	Quzyttir (cetirizine hydrochloride) injection
Pediatric Labeling Approval Date:	October 4, 2019
Application Type/Number:	NDA 211415
Applicant:	JDP Therapeutics, LLC
TTT Record ID:	2023-5798

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Quzyttir (cetirizine hydrochloride) 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 Quzyttir in pediatric patients.

Quzyttir (cetirizine hydrochloride) injection is a histamine-1 receptor antagonist that was initially approved in the U.S. on October 4, 2019. Quzyttir is currently indicated for the treatment of acute urticaria in adults and children 6 months of age and older.

This pediatric postmarketing safety review was prompted by pediatric labeling on initial FDA approval on October 4, 2019. The safety and efficacy of Quzyttir in patients less than 6 months of age has not been established. A pediatric safety review for Quzyttir has not been previously presented to the Pediatric Advisory Committee.

DPV searched FAERS for all serious reports with Quzyttir in pediatric patients less than 18 years of age from October 4, 2019 - July 27, 2023, and did not identify any reports.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Quzyttir (cetirizine hydrochloride) 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 Quzyttir in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY[1]

Quzyttir (cetirizine hydrochloride) injection is a histamine-1 receptor antagonist that was initially approved in the U.S. on October 4, 2019. Quzyttir is currently indicated for the treatment of acute urticaria in adults and children 6 months of age and older.

This pediatric postmarketing safety review was prompted by pediatric labeling on approval for Quzyttir on October 4, 2019. The efficacy of Quzyttir was established in patients aged 6 months – 17 years from extrapolation of efficacy in adults with acute urticaria. The safety of Quzyttir in pediatric patients is supported by information from placebo-controlled clinical trials with oral cetirizine hydrochloride in pediatric patients aged 6 months and older. The safety and efficacy of Quzyttir in patients less than 6 months of age has not been established. A pediatric safety review for Quzyttir has not been previously presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION[1]

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

> ----------CONTRAINDICATIONS----------
> Known hypersensitivity to cetirizine hydrochloride or any of its ingredients, levocetirizine, or hydroxyzine (4)
> ----------WARNINGS AND PRECAUTIONS----------
> Somnolence/Sedation: Exercise caution when driving a car or operating potentially dangerous machinery (5.1)
> ----------ADVERSE REACTIONS----------
> The most common adverse reactions (incidence less than 1%) with QUZYTTIR are dysgeusia, headache, paresthesia, presyncope, dyspepsia, feeling hot, and hyperhidrosis.
>
> Most common adverse reactions (incidence equal to or greater than 2%) with use of oral cetirizine hydrochloride are somnolence, fatigue, dry mouth, pharyngitis, and dizziness. (6)
>
> **8.4 Pediatric Use**
> The safety and efficacy of QUZYTTIR have been established in patients 6 months to 17 years of age. The efficacy of QUZYTTIR for the treatment of acute urticaria down to 6 months of age is based on extrapolation of the efficacy of QUZYTTIR in adults with acute urticaria [See Clinical Studies (14)] and supported by pharmacokinetic data with oral cetirizine hydrochloride (the active ingredient in QUZYTTIR) in patients 6 months to 17 years of age. Based upon the known PK profile of oral cetirizine hydrochloride, the exposure of IV cetirizine hydrochloride in pediatric patients (6 months to 17 years of age) is expected to be similar to the exposure of IV cetirizine hydrochloride in adults at the labeled doses. Extrapolation of

efficacy is based on the likelihood that the disease course, pathophysiology and the drug's effect are similar between these two populations.

The safety of QUZYTTIR in children 6 months to 17 years of age is supported by safety information from placebo-controlled clinical trials with oral cetirizine hydrochloride in patients 6 months of age and older [see Adverse Reactions (6)]. QUZYTTIR demonstrates a higher Cmax compared to oral cetirizine hydrochloride in adults [See Clinical Pharmacology (12.3)]. As QUZYTTIR is indicated for an acute condition administered in a medically supervised setting, the safety for higher Cmax in children 6 months to less than 18 years of age is supported by the safety data from the clinical trial with IV cetirizine hydrochloride in adults [see Adverse Reactions (6)] and available safety information from pediatric overdose cases.

Because of the absence of pharmacokinetic and safety information for cetirizine hydrochloride in children below 6 years of age with impaired renal or hepatic function, the use of QUZYTTIR in this impaired patient population is not recommended [see Dosage And Administration (2)].

The safety and efficacy of QUZYTTIR in patients less than 6 months of age has 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 28, 2023
Time period of search	October 4, 2019† - July 27, 2023
Search type	Drug Safety Analytics Dashboard (DSAD) Quick Query
Product terms	Product Name: Quzyttir NDA: 211415
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Approval date for Quzyttir Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities, NDA=New drug application	

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 October 4, 2019 – July 27, 2023, with Quzyttir.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From October 4, 2019 - July 27, 2023, With Quzyttir			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 18 years)	0 (0)	0 (0)	0 (0)
Pediatrics (0 - < 18 years)	0 (0)	0 (0)	0 (0)

* 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.

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved zero serious pediatric reports from October 4, 2019 - July 27, 2023.

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 Quzyttir in pediatric patients less than 18 years of age from October 4, 2019 - July 27, 2023, and did not identify any reports.

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

5 CONCLUSION

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

6 REFERENCES

1. Quzyttir (cetirizine hydrochloride injection), for intravenous use [Prescribing information]. Lake Forest, IL; TerSera Therapeutics LLC: October, 2019.

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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