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:	April 7, 2025
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Product Name:	Litfulo (ritlecitinib) capsules
Pediatric Labeling Approval Date:	June 23, 2023
Application Type/Number:	NDA 215830
Applicant:	Pfizer, Inc
TTT Record ID:	2025-13614

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Litfulo (ritlecitinib) capsules 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 ritlecitinib in pediatric patients.

Litfulo (ritlecitinib) was initially approved in the U.S. on June 23, 2023, and is currently indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older. The safety and efficacy of ritlecitinib have not been established in pediatric patients under 12 years of age.

This pediatric postmarketing safety review was stimulated by pediatric labeling on June 23, 2023, upon FDA approval of ritlecitinib for the treatment of severe alopecia areata in pediatric patients 12 years and older.

DPV reviewed all U.S. serious FAERS reports with ritlecitinib in pediatric patients less than 18 years of age from June 23, 2023, to March 11, 2025, and identified 24 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 ritlecitinib in pediatric patients less than 18 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Litfulo (ritlecitinib) capsules 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 ritlecitinib in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY[1]

Litfulo (ritlecitinib) is a kinase inhibitor initially approved in the U.S. on June 23, 2023. Ritlecitinib is currently indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older. The safety and efficacy of ritlecitinib have not been established in pediatric patients under 12 years of age.

This pediatric postmarketing safety review was stimulated by pediatric labeling on June 23, 2023, upon FDA approval of ritlecitinib for the treatment of severe alopecia areata in pediatric patients 12 years and older.

Ritlecitinib has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION[1]

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

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), and THROMBOSIS
See full prescribing information for complete boxed warning

- **Increased risk of serious bacterial, fungal, viral and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment if serious infection occurs until the infection is controlled. LITFULO should not be given to patients with active tuberculosis. Test for latent TB before and during therapy; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative, latent TB test. Monitor all patients for signs and symptoms of infection during and after treatment with LITFULO.**
- **Higher rate of all-cause mortality, including sudden cardiovascular death with another Janus kinase inhibitor (JAK) vs. TNF blockers in rheumatoid arthritis (RA) patients. LITFULO is not approved for use in RA patients.**
- **Malignancies were reported in patients treated with LITFULO. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs. TNF blockers in RA patients.**
- **Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in RA patients.**
- **Thrombosis has occurred in patients treated with LITFULO. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs. TNF blockers.**

----------CONTRAINDICATIONS----------

- LITFULO is contraindicated in patients with known hypersensitivity to ritlecitinib or any of its excipients.

----------WARNINGS AND PRECAUTIONS----------

- Hypersensitivity: Discontinue LITFULO if a clinically significant hypersensitivity reaction occurs.
- Laboratory Abnormalities: Perform ALC and platelet counts prior to LITFULO initiation. Treatment interruption or discontinuation are recommended based on ALC and platelet count abnormalities.
- Vaccinations: Avoid use of live vaccines during or shortly prior to LITFULO treatment.

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

- Most common adverse reactions (incidence ≥1%) are headache, diarrhea, acne, rash, urticaria, folliculitis, pyrexia, atopic dermatitis, dizziness, blood creatine phosphokinase increased, herpes zoster, red blood cell count decreased, and stomatitis.

----------USE IN SPECIFIC POPULATIONS----------

8.4 Pediatric Use

The safety and effectiveness of LITFULO for the treatment of alopecia areata have been established in pediatric patients ages 12 years and older. A total of 181 pediatric patients ages 12 to <18 years were enrolled in alopecia areata clinical trials, with 105 pediatric patients ages 12 to <18 years with alopecia areata randomized in a pivotal, double-blind, placebo-controlled trial (Trial AA-I). Efficacy was consistent between the pediatric patients and adults. The adverse reaction profile in the pediatric patients was similar to adults.

The safety and efficacy of LITFULO have not been established in pediatric patients under 12 years of age.

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	March 12, 2025
Time period of search	June 23, 2023† - March 11, 2025
Search type	RxLogix Pediatric Focused Review Alert
Product terms	Product Active Ingredient: ritlecitinib; ritlecitinib tosylate
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.
† U.S. approval date for Litfulo (ritlecitinib).
‡ 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.
Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities; USA=United States of America

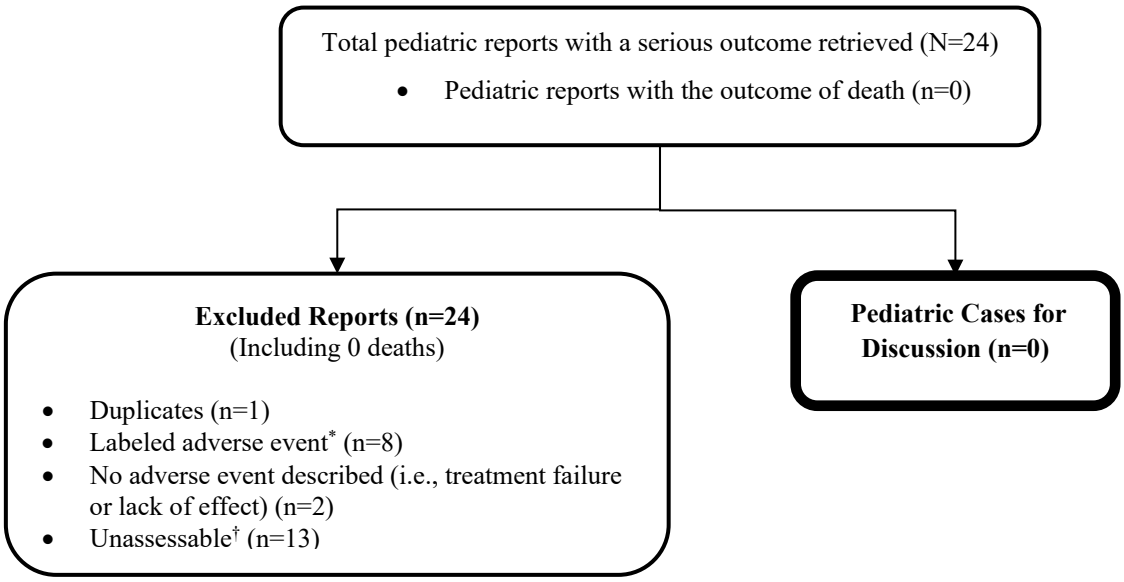
3 RESULTS

3.1 FAERS

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

Our FAERS search retrieved 24 U.S. serious pediatric reports for patients less than 18 years old from June 23, 2023, through March 11, 2025. We reviewed all U.S. FAERS pediatric reports with a serious outcome. We excluded all 24 reports from the case series for the reasons listed in Figure 1.

Figure 1. Selection of U.S. Serious Pediatric Cases with Ritlecitinib



* 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 ritlecitinib in pediatric patients less than 18 years of age from June 23, 2023, to March 11, 2025, and identified 24 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 ritlecitinib in pediatric patients less than 18 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Litfulo Product Label. June 2023. Available from Drugs@FDA: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215830s000lbl.pdf

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.