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

Pediatric Postmarketing Pharmacovigilance Review

Date:	May 28, 2025
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Product Name:	Rapivab (peramivir)
Pediatric Labeling Approval Date:	January 28, 2021
Application Type/Number:	NDA 206426
Applicant:	BioCryst Pharmaceuticals, Inc.
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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Rapivab (peramivir) 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 peramivir in pediatric patients.

Rapivab (peramivir) is an influenza virus neuraminidase inhibitor and was initially approved in the U.S. on December 19, 2014. Peramivir is currently indicated for the treatment of acute uncomplicated influenza in patients 6 months and older who have been symptomatic for no more than two days.

This pediatric postmarketing safety review was prompted by the pediatric labeling on January 28, 2021, which expanded the indication from use in patients aged 2 years and older to use in patients aged 6 months and older.

On June 17, 2019, DPV completed a review of postmarketing adverse event reports with a serious outcome for peramivir in pediatric patients in preparation for a Pediatric Advisory Committee (PAC). DPV's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with peramivir. On September 19, 2019, DPV's evaluation was presented to the PAC via webposting.

DPV searched FAERS for all U.S. serious reports with peramivir in pediatric patients less than 18 years of age from May 1, 2019, through May 1, 2025, and did not identify any reports.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Rapivab (peramivir) 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 peramivir in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Rapivab (peramivir) is an influenza virus neuraminidase inhibitor and was initially approved in the U.S. on December 19, 2014.[1] Peramivir is currently indicated for the treatment of acute uncomplicated influenza in patients 6 months and older who have been symptomatic for no more than two days.[1]

This pediatric postmarketing safety review was prompted by pediatric labeling on January 28, 2021, which expanded the indication from use in patients aged 2 years and older to use in patients aged 6 months and older.[2]

On June 17, 2019, DPV completed a review of postmarketing adverse event reports with a serious outcome for peramivir in pediatric patients.[3] DPV's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with peramivir. On September 19, 2019, DPV's evaluation was presented to the Pediatric Advisory Committee via webposting.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

> ----------CONTRAINDICATIONS----------
> Patients with known serious hypersensitivity or anaphylaxis to peramivir or any component of RAPIVAB (4)
>
> ----------WARNINGS AND PRECAUTIONS----------
> • Cases of anaphylaxis and serious skin/hypersensitivity reactions such as Stevens-Johnson syndrome and erythema multiforme have occurred with RAPIVAB. Discontinue RAPIVAB and initiate appropriate treatment if anaphylaxis or serious skin reaction occurs or is suspected. (5.1)
> • Neuropsychiatric events: Patients with influenza may be at an increased risk of hallucinations, delirium, and abnormal behavior early in their illness. Monitor for signs of abnormal behavior. (5.2)
>
> ----------ADVERSE REACTIONS----------
> Most common adverse reaction (incidence >2%) is diarrhea. (6)
>
> *Pediatric Use*
>
> The safety and effectiveness of RAPIVAB for the treatment of influenza has been established in pediatric patients 6 months to 17 years of age. Use of RAPIVAB for this indication is supported by evidence from adequate and well-controlled trials of RAPIVAB in adults with additional data from Study 305, a randomized, active-controlled trial of 130 adolescent and pediatric subjects with acute uncomplicated influenza who received open-label treatment with a single dose of RAPIVAB or 5 days of treatment with oseltamivir administered within 48 hours of onset of symptoms of influenza

[see Dosage and Administration (2.1, 2.2, 2.3), Adverse Reactions (6.1), Clinical Pharmacology (12.3), Clinical Studies (14.2)]. Study 305 included:

- 13 to 17 years of age: 21 subjects treated with RAPIVAB 600 mg
- 6 months to 12 years of age: 86 subjects treated with RAPIVAB 12 mg/kg (up to a maximum dose of 600 mg)

Safety and effectiveness of RAPIVAB in pediatric patients less than 6 months of age have not been established. No data are available for RAPIVAB use in pediatric patients 6 months to less than 2 years with creatinine clearance <50 mL/min to inform a recommendation for dosage adjustment *[see Dosage and Administration (2.2), Clinical Pharmacology (12.3)]*.

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	May 2, 2025
Time period of search	May 1, 2019† - May 1, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: peramivir anhydrous, peramivir
MedDRA search terms (Version 27.1)	All Preferred Terms
Other criteria	Case Seriousness: Serious‡ Country Derived: USA
* See Appendix A for a description of the FAERS database. † The FAERS search period for the most recently completed DPV pediatric postmarketing pharmacovigilance review for Rapivab ended on April 30, 2019. ‡ 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 no U.S. serious pediatric reports for patients less than 18 years old from May 1, 2019, through May 1, 2025.

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 searched FAERS for all U.S. serious reports with peramivir in pediatric patients less than 18 years of age from May 1, 2019, through May 1, 2025, and did not identify any reports.

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

5 CONCLUSION

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

6 REFERENCES

1. Rapivab (peramivir) injection [package insert]. Durham, NC: BioCryst Pharmaceuticals, Inc. January 2024.
2. U.S. Food and Drug Administration. Supplemental NDA Approval Letter for NDA 206426 (S-007), Rapivab (peramivir); injection. January 28, 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2021/206426Orig1s007ltr.pdf.
3. Jancel T, Kim I, Cao K, Diak IL. Rapivab Pediatric Postmarketing Pharmacovigilance Review. June 17, 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.