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Pediatric Postmarketing Pharmacovigilance Review

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EXECUTIVE SUMMARY

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

Veklury (remdesivir) is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleotide analog RNA polymerase inhibitor, initially FDA approved on October 22, 2020. Remdesivir is currently indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (birth to less than 18 years of age weighing at least 1.5 kg) who are: hospitalized, *or* not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization and death.

This pediatric postmarketing safety review was prompted by the pediatric labeling on February 28, 2024, that expanded the use of remdesivir for the treatment of COVID-19 to include pediatric patients from birth to less than 28 days of age weighing at least 1.5 kg to less than 3 kg.

DPV reviewed all U.S. serious FAERS reports with remdesivir in pediatric patients less than 18 years of age from October 2, 2023, through March 2, 2026. Of the 24 reports reviewed, DPV included 1 case in the case series. This single case described persistent bradycardia temporally associated with remdesivir, however, the case lacked important clinical information for adequate assessment. The findings in this case were consistent with those from prior FDA assessments, which have found insufficient evidence of a causal association between remdesivir and bradycardia.

Overall, there were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with remdesivir in pediatric patients less than 18 years of age. DPV will continue routine pharmacovigilance monitoring for remdesivir.

1 INTRODUCTION

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

1.1 PEDIATRIC REGULATORY HISTORY

Veklury (remdesivir) is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleotide analog RNA polymerase inhibitor and was initially FDA approved on October 22, 2020.¹ Remdesivir is currently indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (birth to less than 18 years of age weighing at least 1.5 kg) who are: hospitalized, *or* not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization and death.²

This pediatric postmarketing safety review was prompted by pediatric labeling on February 28, 2024, that expanded the use of remdesivir for the treatment of COVID-19 to include pediatric patients from birth to less than 28 days of age weighing at least 1.5 kg to less than 3 kg.³ Data to support use in this population is included in the *Pediatric Use* subsection of labeling (see **Section 1.2**).

On January 19, 2024, DPV completed a review of postmarketing adverse event reports with a serious outcome for remdesivir in pediatric patients.⁴ DPV's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with remdesivir. On September 26, 2024, DPV's evaluation was presented to the Pediatric Advisory Committee via webposting.

1.2 RELEVANT LABELED SAFETY INFORMATION

The remdesivir labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional remdesivir labeling information, please refer to the full prescribing information.²

-----CONTRAINDICATIONS-----

VEKLURY is contraindicated in patients with a history of clinically significant hypersensitivity reactions to VEKLURY or any components of the product. (4)

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

- Hypersensitivity including infusion-related and anaphylactic reactions: Hypersensitivity reactions have been observed during and following administration of VEKLURY. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent signs and symptoms of hypersensitivity. Monitor patients during infusion and observe patients for at least one hour after infusion is complete for signs and symptoms of hypersensitivity as clinically appropriate. If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue administration of VEKLURY and initiate appropriate treatment. (5.1)

- Increased risk of transaminase elevations: Transaminase elevations have been observed in healthy volunteers and have also been reported in patients with COVID-19 who received VEKLURY. Perform hepatic laboratory testing in all patients before starting VEKLURY and while receiving VEKLURY as clinically appropriate. Consider discontinuing VEKLURY if ALT levels increase to greater than 10 times the upper limit of normal. Discontinue VEKLURY if ALT elevation is accompanied by signs or symptoms of liver inflammation. (5.2)
- Risk of reduced antiviral activity when coadministered with chloroquine phosphate or hydroxychloroquine sulfate: Coadministration of VEKLURY and chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on data from cell culture experiments demonstrating a potential antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of VEKLURY. (5.3)

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

The most common adverse reactions (incidence greater than or equal to 5%, all grades) observed with treatment with VEKLURY are nausea, ALT increased, and AST increased. (6.1)

8.4 Pediatric Use

The safety and effectiveness of VEKLURY for the treatment of COVID-19 have been established in pediatric patients from birth to less than 18 years of age and weighing at least 1.5 kg, who are:

- Hospitalized, or
- Not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

Use in this age group is supported by the following:

- Trials in adults [*see Clinical Studies (14.1, 14.2, 14.3, 14.4, 14.5)*]
- An open-label trial (Study 5823) in 58 hospitalized pediatric subjects [*see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.6)*].

Use of VEKLURY in pediatric patients from birth to less than 18 years of age and weighing at least 1.5 kg is supported by Study 5823 where 58 hospitalized pediatric subjects were treated with weight-based VEKLURY for up to 10 days in the following cohorts:

- *Cohorts 1-4, 8; infants, children, and adolescents:* Subjects ≥ 12 years and weighing ≥ 40 kg (n=12); subjects < 12 years and weighing ≥ 40 kg (n=5); subjects ≥ 28 days and weighing ≥ 20 to < 40 kg (n=12); subjects ≥ 28 days and weighing ≥ 12 to < 20 kg (n=12); and subjects ≥ 28 days and weighing ≥ 3 to < 12 kg (n=12);
- *Cohorts 5-7; neonates and infants:* Subjects 14 to < 28 days old, GA > 37 weeks, and weighing ≥ 2.5 kg (n=3); subjects < 14 days old, GA > 37 weeks, and weighing ≥ 2.5 kg at birth (n=1); and subjects < 56 days old, GA ≤ 37 weeks, and weighing ≥ 1.5 kg at birth (n=1).

The safety and pharmacokinetic results in pediatric subjects were similar to those in adults [*see Adverse Reactions (6.1), Clinical Pharmacology (12.3), Clinical Studies (14.6)*].

Use of VEKLURY in pediatric patients weighing at least 40 kg is further supported by a clinical trial of VEKLURY in non-hospitalized subjects that included 3 pediatric subjects 12 years and older, and by clinical trials in hospitalized subjects that included 30 adult subjects weighing 40 to 50 kg. The safety in this weight group was comparable to adult subjects weighing greater than 50 kg. Thirty-nine pediatric patients 12 years and older and weighing at least 40 kg received VEKLURY in a compassionate use program in hospitalized subjects; the available clinical data from these patients are limited [*see Adverse Reactions (6.1) and Clinical Studies (14)*].

Use of VEKLURY in pediatric patients with renal impairment is supported by safety data in adults [see *Adverse Reactions* (6.1), *Use in Specific Populations* (8.6)]. Limited data are available regarding the safety of VEKLURY in pediatric patients with mild or moderate renal impairment. No data are available regarding the safety of VEKLURY in pediatric patients with severe renal impairment. In adults with severe renal impairment, including those requiring dialysis, exposures of GS-441524 and GS-704277, the metabolites of remdesivir, and betadex sulfobutyl ether sodium (SBECD) are increased [see *Clinical Pharmacology* (12.3)]. VEKLURY contains SBECD which, when administered intravenously, is eliminated through glomerular filtration and therefore when administered to pediatric patients with renal immaturity or renal impairment, may result in higher exposure to SBECD.

The safety and effectiveness of VEKLURY have not been established in pediatric patients weighing less than 1.5 kg.

2 METHODS AND MATERIALS

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

Table 1. FAERS Search Strategy*

Date of search	March 3, 2026
Time period of search	October 2, 2023 [†] - March 2, 2026
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	PAI: Remdesivir
MedDRA search terms (Version 28.1)	All Preferred Terms

* 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 remdesivir ended on October 1, 2023.

Abbreviation: PAI=Product Active Ingredient, MedDRA=Medical Dictionary for Regulatory Activities

3 RESULTS

3.1 SELECTION OF U.S. SERIOUS PEDIATRIC CASES IN FAERS

Our FAERS search retrieved 24 U.S. serious^a pediatric reports for patients less than 18 years old from October 2, 2023, through March 2, 2026,^b including 10 reports with the outcome of death. We excluded 23 reports from the case series for the reasons described below:

- Duplicates (n=8, including 6 deaths)
- Labeled adverse event not representing increased severity (n=1)
- Adverse event more likely due to concomitant medications or comorbidities (n=3, including 2 deaths)
- No adverse event described (i.e., treatment failure or lack of effect) (n=3, including 1 death)

^a 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.

^b Includes one pediatric report that was identified among reports not coded with an age.

- Unassessable^c (n=8, including 1 death)

Ten excluded U.S. FAERS reports described fatal outcomes. After accounting for duplicate reports (n=6), we identified 4 unique cases describing fatal outcomes. None of the deaths were determined to be attributed to remdesivir. Three cases described death secondary to complications from primary disease or other medical conditions (COVID-19-related death n=2; disseminated tuberculosis n=1). One case lacked sufficient clinical information to understand events that led to death or perform a causality assessment with remdesivir.

After excluding reports as described above, one non-fatal case remained for discussion.

Appendix B contains a line listing of the one pediatric case in the case series.

3.2 SUMMARY OF U.S. FATAL PEDIATRIC CASES (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.3 SUMMARY OF U.S. SERIOUS NON-FATAL PEDIATRIC CASES (N=1)

We identified one U.S. pediatric FAERS case with remdesivir reporting a non-fatal serious outcome. The case reported bradycardia and this case is summarized below:

FAERS Case #24900473, United States, Initial FDA Received Date: January 29, 2025, Expedited Report, Serious Outcome: Hospitalization, Other Serious

This FAERS case, from an abstract in the medical literature,⁵ describes a 15-year-old female with a past medical history of asthma and hyperinsulinemia who was hospitalized for acute hypoxic respiratory failure secondary to COVID-19 pneumonia. She was started on ceftriaxone, azithromycin, and a 10-day course of remdesivir. On the third day of her hospitalization, she developed asymptomatic sinus bradycardia with a heart rate nadir of 30-40 bpm. On the fifth day of her hospitalization, she completed her course of remdesivir and was discharged four days later, with a heart rate of 47 bpm at the time of discharge. That night, she returned to the emergency department with acute onset of lightheadedness and blurry vision at home secondary to orthostatic hypotension and bradycardia. Vitals on presentation were heart rate 48 bpm, temperature 36.1°C, respirations 24/min, blood pressure 119/50 mmHg, and SpO2 99% on room air. Physical exam was reported to be unremarkable. EKG showed sinus bradycardia with a PR interval of 124 ms and QTc of 406 ms and echocardiogram showed normal cardiac anatomy and function. She was diagnosed with “persistent RDV[remdesivir]-associated bradycardia” and was discharged home with a Holter monitor and planned follow-up with cardiology. The bradycardia had resolved by her follow-up visit two weeks later.

DPV Reviewers’ Comments: Bradycardia is labeled for remdesivir as a symptom of hypersensitivity reactions, including infusion-related reactions, however, it is not clear in this

^c Unassessable reports are those that 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.

case if the bradycardia initially started during a remdesivir infusion. Nonetheless, we acknowledge subsequent persistence of the bradycardia throughout the hospitalization. We additionally note symptoms (i.e., lightheadedness, blurry vision) attributed by the authors to bradycardia in this case, however, the symptoms did not occur with the bradycardia until after completion of the remdesivir course and discharge from the hospital. Although the case initially described a 10-day course of remdesivir, it is later stated that remdesivir was completed on day five. The reported episode of symptomatic bradycardia therefore likely occurred four days after remdesivir was discontinued, which is nearing the time at which remdesivir would be expected to be cleared (i.e., ~5 days as $t_{1/2}$ for the GS-441524 metabolite is 27 hours). Details of her hospital course including clinical status and concomitant medications besides anti-infectives were not reported, limiting our assessment of other potential causes for the bradycardia. Additionally, the reported heart rate at the time of the symptoms (i.e., 48 bpm) is higher than the patient's nadir heart rate (i.e., 30-40 bpm), at which time the patient was asymptomatic. Considering this and that the symptoms occurred immediately post-discharge, it is possible that the symptoms (i.e., lightheadedness, blurry vision) could be due to deconditioning from severe COVID-19 infection and hospitalization rather than the bradycardia. Bradycardia with remdesivir was previously evaluated by multidisciplinary FDA staff in an Integrated Safety Assessment (ISA) in October 2021,⁶ and it was determined that at that time, there was insufficient evidence of a causal association between remdesivir and bradycardia. No regulatory action was recommended based on the ISA and routine pharmacovigilance has continued. Subsequent DPV memorandums, including adverse event summaries for remdesivir completed in January 2022⁷ and March 2022⁸, evaluated bradycardia cases and had findings consistent with the ISA. Bradycardia cases were also identified in the January 2024 pediatric postmarketing adverse event review for remdesivir;⁴ similar to the bradycardia cases in that review, the findings from the case identified in this review are consistent with the findings in prior FDA assessments.

4 DISCUSSION

DPV reviewed all U.S. serious FAERS reports with remdesivir in pediatric patients less than 18 years of age from October 2, 2023, through March 2, 2026. Of the 24 reports reviewed, DPV included 1 case in the case series. This single case described persistent bradycardia temporally associated with remdesivir, however, the case lacked important clinical information for adequate assessment. The findings in this case were consistent with those from prior FDA assessments, which have found insufficient evidence of a causal association between remdesivir and bradycardia.

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

5 CONCLUSION

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

6 REFERENCES

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https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/214787s026lbl.pdf. Accessed March 24, 2026.
- ⁴ McCartan K, Kim I, Kapoor R, Diak IL. Veklury (remdesivir) Pediatric Postmarketing Pharmacovigilance Review. January 2024.
- ⁵ Mancha G, Corrado AC, Wilkerson MK. Time to Slow Down: A Deeper Look into Remdesivir-Associated Bradycardia. *Chest*. October 2022. 162(4): A2030-A2031.
- ⁶ Gada N, Mishra P, et al. Newly Identified Safety Signal (NISS) Integrated Safety Assessment: Remdesivir and Bradycardia. October 26, 2021.
- ⁷ McCartan K, Kapoor R, Diak IL. Veklury (remdesivir) Summary of Adverse Events Pharmacovigilance Memorandum. January 2022.
- ⁸ McCartan K, Kapoor R, Diak IL. Veklury (remdesivir) Summary of Adverse Events Pharmacovigilance Memorandum. March 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 is consistent with international safety reporting guidance issued by the International Council on Harmonisation and adheres to FDA guidance on adverse event reporting. 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.

7.2 APPENDIX B. FAERS LINE LISTING OF THE PEDIATRIC CASE SERIES (N=1)

	FAERS Case #	Version #	Initial FDA Received Date	Manufacturer Control # or Central Triage Unit #	Case Type	Age (years)	Sex	Country Derived	Serious Outcomes*
1	24900473	2	1/29/2025	US-GILEAD- 2022-0600972	Expedited	15	Female	USA	HO, OT
*As per 21 CFR 314.80, the regulatory definition of serious is any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, a congenital anomaly/birth defect, or other serious important medical events. Those that are blank were not marked as serious (per the previous definition) by the reporter and are coded as non-serious. A case can have more than one serious outcome. The coded outcomes are report-level outcomes (i.e., they reflect any serious outcomes for any adverse events coded to a Preferred Term in the FAERS report). Therefore, a serious outcome may not apply to all adverse events in a FAERS report. A review of the FAERS report narrative is necessary to determine adverse-event-level outcomes and any association to a suspect product. Abbreviations: HO=hospitalization, OT=other medically significant, USA=United States of America									