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: May 15, 2025

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Product Name	Pediatric Labeling Approval Date	Application Type/Numbers	Applicant
Selzentry (maraviroc) tablets	October 30, 2020	NDA 022128	ViiV Healthcare
Selzentry (maraviroc) oral solution	October 30, 2020	NDA 208984	ViiV Healthcare

TTT Record ID: 2025-14425

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Selzentry (maraviroc) 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). This review focuses on United States (U.S.) serious unlabeled adverse events associated with maraviroc in pediatric patients.

Selzentry (maraviroc) is a CCR5 co-receptor antagonist, which selectively binds to the human chemokine receptor CCR5, preventing the interaction of human immunodeficiency virus type 1 (HIV-1) gp120 and CCR5 necessary for CCR5-tropic HIV-1 to enter cells. Selzentry was initially approved in the U.S. on August 6, 2007, and is currently available as an oral tablet and oral solution. Selzentry is currently indicated in combination with other antiretroviral agents for the treatment of only CCR5-tropic HIV-1 infection in adults and pediatric patients weighing at least 2 kg. Selzentry is not recommended in patients with dual/mixed- or CXC4-tropic HIV-1.

This pediatric postmarketing safety review was prompted by pediatric labeling on October 30, 2020, which expanded the indication to include treatment of HIV-1 infection in pediatric patients weighing at least 2 kg and provided dosing recommendations for pediatric patients weighing 10 kg to less than 30 kg when used with noninteracting concomitant medications.

On December 20, 2018, DPV completed a review of postmarketing adverse event reports with a serious outcome for maraviroc in pediatric patients. DPV's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with maraviroc. On March 28, 2019, DPV's evaluation was presented to the Pediatric Advisory Committee via webposting.

DPV reviewed all U.S. serious FAERS reports with maraviroc in pediatric patients less than 18 years of age from October 1, 2018, through April 30, 2025, and identified four 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 maraviroc in pediatric patients less than 18 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Selzentry (maraviroc) 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). This review focuses on United States (U.S.) serious unlabeled adverse events associated with maraviroc in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Selzentry (maraviroc) is a CCR5 co-receptor antagonist, which selectively binds to the human chemokine receptor CCR5, preventing the interaction of human immunodeficiency virus type 1 (HIV-1) gp120 and CCR5 necessary for CCR5-tropic HIV-1 to enter cells.[1] Selzentry was initially approved in the U.S. on August 6, 2007, and is currently available as an oral tablet and oral solution.[1] Selzentry is currently indicated in combination with other antiretroviral agents for the treatment of only CCR5-tropic HIV-1 infection in adults and pediatric patients weighing at least 2 kg.[1] Selzentry is not recommended in patients with dual/mixed- or CXC4-tropic HIV-1.

This pediatric postmarketing safety review was prompted by pediatric labeling on October 30, 2020, which expanded the indication to include treatment of HIV-1 infection in pediatric patients weighing at least 2 kg and provided dosing recommendations for pediatric patients weighing 10 kg to less than 30 kg when used with noninteracting concomitant medications.[2]

On December 20, 2018, DPV completed a review of postmarketing adverse event reports with a serious outcome for maraviroc in pediatric patients. DPV's evaluation did not identify any new safety concerns and recommended return to routine monitoring for adverse events with maraviroc.[3] On March 28, 2019, DPV's evaluation was presented to the Pediatric Advisory Committee via webposting.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

WARNING: HEPATOTOXICITY

See full prescribing information for complete boxed warning.

- **Hepatotoxicity has been reported which may be preceded by severe rash or other features of a systemic allergic reaction (e.g., fever, eosinophilia, or elevated IgE). (5.1)**
- **Immediately evaluate patients with signs or symptoms of hepatitis or allergic reaction. (5.1)**

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

- SELZENTRY is contraindicated in patients with severe renal impairment or end-stage renal disease (ESRD) (CrCl less than 30 mL per minute) who are concomitantly taking potent CYP3A inhibitors or inducers. (4)

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

- Hepatotoxicity accompanied by severe rash or systemic allergic reaction, including potentially life-threatening events, has been reported. Hepatic laboratory parameters including ALT, AST, and bilirubin should be obtained prior to starting SELZENTRY and at other time points during treatment as clinically indicated. If rash or symptoms or signs of hepatitis or allergic reaction develop, hepatic laboratory parameters should be monitored and discontinuation of treatment should be considered. When administering SELZENTRY to patients with pre-existing liver dysfunction or who are co-infected with hepatitis B and/or C virus, additional monitoring may be warranted. (5.1)
- Severe and potentially life-threatening skin and hypersensitivity reactions have been reported in patients taking SELZENTRY. This includes cases of Stevens-Johnson syndrome, hypersensitivity reaction, and toxic epidermal necrolysis. Immediately discontinue SELZENTRY and other suspected agents if signs or symptoms of severe skin or hypersensitivity reactions develop and monitor clinical status, including liver aminotransferases, closely. (5.2)
- More cardiovascular events, including myocardial ischemia and/or infarction, were observed in treatment-experienced subjects who received SELZENTRY. Additional monitoring may be warranted. (5.3)
- If patients with severe renal impairment or ESRD receiving SELZENTRY (without concomitant CYP3A inducers or inhibitors) experience postural hypotension, the dose of SELZENTRY should be reduced from 300 mg twice daily to 150 mg twice daily. (5.3)

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

- The most common adverse events in treatment-experienced adult subjects (greater than 8% incidence) which occurred at a higher frequency compared with placebo are upper respiratory tract infections, cough, pyrexia, rash, and dizziness. (6.1)
- The most common adverse events in treatment-naive adult subjects (greater than 8% incidence) which occurred at a higher frequency than the comparator arm are upper respiratory tract infections, bronchitis, flatulence, bloating and distention, upper respiratory tract signs and symptoms, and gastrointestinal atonic and hypomotility disorders. (6.1)
- The most common adverse reactions in treatment-experienced pediatric subjects (greater than or equal to 3% incidence) are vomiting, abdominal pain, diarrhea, nausea, and dizziness. (6.1)

8.4 Pediatric Use

The safety and efficacy of SELZENTRY have been established in pediatric patients aged from birth to less than 18 years. The use of SELZENTRY in pediatric patients was supported by pharmacokinetic and safety data described below and by previous demonstration of efficacy in adult patients *[see Indications and Usage (1)], Dosage and Administration (2.4)]*.

HIV-1–Infected Pediatric Patients Aged 2 to Less Than 18 Years: The safety, pharmacokinetic profile, and antiviral activity of SELZENTRY were evaluated in treatment-experienced, CCR5-tropic, HIV-1–infected pediatric subjects aged 2 to less than 18 years weighing at least 10 kg in an open-label, multicenter clinical trial, A4001031 *[see Adverse Reactions (6.1), Clinical Studies (14.2)]*. Pharmacokinetics were evaluated in a total of 98 pediatric subjects: 85 subjects received SELZENTRY and concomitant medications that included potent CYP3A inhibitors with or without potent CYP3A inducers, 10 subjects received SELZENTRY and noninteracting medications (not containing potent CYP3A inhibitors or potent CYP3A inducers), and three subjects received SELZENTRY and medications that included potent CYP3A inducers without potent CYP3A inhibitors *[see Clinical Pharmacology (12.3)]*.

HIV-1–Infected Pediatric Patients Aged Older Than 6 Weeks to Less Than 2 Years: No clinical trials have been conducted in children aged older than 6 weeks to less than 2 years. Dosing recommendations for SELZENTRY in this population when concomitantly receiving noninteracting medications are based on population pharmacokinetic modeling and simulation only *[see Dosage and Recommendations (2.4), Clinical Pharmacology (12.3)]*.

HIV-1–Infected Neonates Aged from Birth to 6 Weeks: The recommendation of SELZENTRY for the treatment of HIV-1 infection in this pediatric population is based on safety and pharmacokinetic data obtained from clinical trial IMPAACT P2007. In IMPAACT P2007, the safety and pharmacokinetic profiles of SELZENTRY were evaluated in full-term HIV-1–exposed neonates (born to HIV-1–infected mothers) aged from birth through 6 weeks *[see Adverse Reactions (6.1)]*. Pharmacokinetics were evaluated in 38 of 47 enrolled neonates who received SELZENTRY as a

single dose (n = 13) or multiple doses (n = 25) up to 6 weeks of age concomitantly with other antiretrovirals (mostly zidovudine and/or nevirapine) with or without maternal exposure to efavirenz. HIV-1 status was assessed by nucleic acid test at birth, Week 6, and Week 16; all 47 enrolled neonates were HIV-1 negative at completion of the study *[see Clinical Pharmacology (12.3)]*.

There are insufficient data to make dosing recommendations for use of SELZENTRY in pediatric patients concomitantly receiving potent CYP3A inhibitors and weighing less than 10 kg, or in any pediatric patients concomitantly receiving potent CYP3A inducers without a potent CYP3A inhibitor *[see Dosage and Administration (2.4, 2.5)]*.

SELZENTRY is not recommended in pre-term neonates or in pediatric patients weighing less than 2 kg.

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 1, 2025
Time period of search	October 1, 2018† - April 30, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product active ingredient: maraviroc
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 maraviroc ended on September 30, 2018.
‡ 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

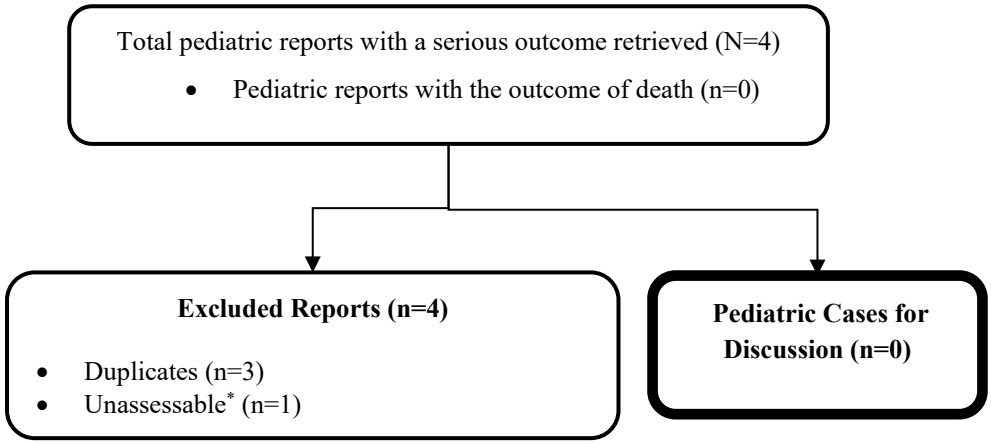
3 RESULTS

3.1 FAERS

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

Our FAERS search retrieved four U.S. serious pediatric reports for patients less than 18 years old from October 1, 2018, through April 30, 2025. We reviewed all U.S. FAERS pediatric reports with a serious outcome. We excluded all four reports from the case series for the reasons listed in **Figure 1**.

Figure 1. Selection of U.S. Serious Pediatric Cases With Maraviroc



* 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 maraviroc in pediatric patients less than 18 years of age from October 1, 2018, through April 30, 2025, and identified four 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 maraviroc in pediatric patients less than 18 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Selzentry (maraviroc) [package insert]. Research Triangle Park, NC: ViiV Healthcare. October 2020.
2. U.S. Food and Drug Administration. Supplemental NDA Approval Letter for NDA 022128 (S-019) and NDA 208984 (S-002), Selzentry (maraviroc); tablet and oral solution. October 20, 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/022128Orig1s019;%20208984Orig1s002ltr.pdf.

3. Gish P, Kim I, Cao K, Diak IL. Selzentry Pediatric Postmarketing Pharmacovigilance Review. December 20, 2018. Available at: https://www.fda.gov/media/123727/download.

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.