Department of Health and Human Services
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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 2, 2025
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Product Names:	Myrbetriq extended-release tablets, Myrbetriq granules (mirabegron)
Pediatric Labeling Approval Date:	March 25, 2021
Application Type/Numbers:	NDA 202611, 213801
Applicant:	Astellas Pharma Global Development, Inc.
TTT Record ID:	2025-12775

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Myrbetriq (mirabegron) 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 and the Pediatric Research Equity Act. This review focuses on United States (U.S.) serious unlabeled adverse events associated with mirabegron in pediatric patients.

Myrbetriq (mirabegron extended-release tablets) is a beta-3 adrenergic agonist and was initially approved in the U.S. on June 28, 2012.[1] Myrbetriq is currently indicated for overactive bladder in adult patients and neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older and weighing 35 kg or more.[1] Myrbetriq granules (mirabegron for extended-release oral suspension) was approved in the U.S. on March 25, 2021. Myrbetriq granules is indicated for the treatment of NDO in pediatric patients aged 3 years and older.[1] For the purposes of this document, we will refer to Myrbetriq and Mybetriq granules by the product active ingredient, mirabegron.

This pediatric postmarketing safety review was prompted by the pediatric labeling change on March 25, 2021 for mirabegron extended-release tablets, which included the new pediatric indication for NDO in patients 3 years of age and older. Additionally, a new formulation of mirabegron (i.e., extended-release oral suspension) for use in pediatric patients was approved at the same time.

DPV reviewed all U.S. serious FAERS reports with mirabegron in pediatric patients less than 18 years of age from June 28, 2012 through February 12, 2025, and identified 6 reports; however, all reports were excluded from further discussion because they did not refer to a pediatric patient, described labeled adverse events, or did not contain suffient information to assess causality.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Myrbetriq (mirabegron) 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 and the Pediatric Research Equity Act. This review focuses on United States (U.S.) serious unlabeled adverse events associated with mirabegron in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Myrbetriq (mirabegron extended-release tablets) is a beta-3 adrenergic agonist and was initially approved in the U.S. on June 28, 2012.[1] Myrbetriq is currently indicated for overactive bladder in adult patients and neurogenic detrusor overactivity (NDO) in pediatric patients aged 3 years and older and weighing 35 kg or more.[1] Myrbetriq granules (mirabegron for extended-release oral suspension) was approved in the U.S. on March 25, 2021. Myrbetriq granules is indicated for the treatment of NDO in pediatric patients aged 3 years and older.[1] For the purposes of this document, we will refer to Myrbetriq and Mybetriq granules by the product active ingredient, mirabegron.

This pediatric postmarketing safety review was prompted by the pediatric labeling change on March 25, 2021 for mirabegron extended-release tablets, which included the new pediatric indication for NDO in patients 3 years of age and older. Additionally, a new formulation of mirabegron (i.e., extended-release oral suspension) for use in pediatric patients was approved at the same time.

A pediatric safety review for mirabegron has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

---------- **CONTRAINDICATIONS** ----------
Hypersensitivity to mirabegron or any inactive ingredients.

---------- **WARNINGS AND PRECAUTIONS** ----------
• Increases in Blood Pressure: Can increase blood pressure in adult or pediatric patients. Periodically monitor blood pressure, especially in hypertensive patients. MYRBETRIQ/MYRBETRIQ Granules are not recommended in patients with severe uncontrolled hypertension.
• Urinary Retention in Patients With Bladder Outlet Obstruction and in Patients Taking Muscarinic Antagonist Drugs for Overactive Bladder (OAB): Administer with caution in these patients because of risk of urinary retention.
• Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with mirabegron.

---------- **ADVERSE REACTIONS** ----------
• Most commonly reported adverse reactions with MYRBETRIQ monotherapy in adult patients with OAB (> 2% and > placebo) were hypertension, nasopharyngitis, urinary tract infection (UTI), and headache.

• Most commonly reported adverse reactions with MYRBETRIQ, in combination with solifenacin succinate in adult patients with OAB (> 2% and > placebo and > comparator), were dry mouth, urinary tract infection, constipation, and tachycardia.
• Most commonly reported adverse reactions with MYRBETRIQ/MYRBETRIQ Granules in pediatric patients with NDO (≥ 3%) were UTI, nasopharyngitis, constipation, and headache.

8.4 Pediatric Use
The safety and effectiveness have been established only for the following pediatric indications:
• MYRBETRIQ: Treatment of neurogenic detrusor overactivity (NDO) in pediatric patients 3 years of age and older and weighing 35 kg or more.
• MYRBETRIQ Granules: Treatment of NDO in pediatric patients 3 years of age and older.

The safety and effectiveness of MYRBETRIQ/MYRBETRIQ Granules in pediatric patients aged 3 years and older have been established for the treatment of NDO and the information on this use is discussed throughout the labeling. Use of MYRBETRIQ/MYRBETRIQ Granules for this indication is supported by evidence from a 52-week, open-label, baseline-controlled, multicenter, dose titration trial in pediatric patients 3 years of age and older with NDO (Study 9). Results showed an improvement from baseline in maximum cystometric (bladder) capacity with MYRBETRIQ/MYRBETRIQ Granules use. The most commonly reported adverse reactions in Study 9 (≥3%) were UTI, nasopharyngitis, constipation, and headache. Increased mean systolic and diastolic blood pressures with use of MYRBETRIQ/MYRBETRIQ Granules occurred in patients less than 12 years of age with larger increases in patients younger than 8 years of age.

Take MYRBETRIQ/MYRBETRIQ Granules with food to reduce potential exposure-related risks, such as increased heart rate, as predicted by modeling of vital signs data in Study 9.

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	February 13, 2025
Time period of search	June 28, 2012† - February 12, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product term	Product active ingredient: Mirabegron
MedDRA search terms (Version 27.1)	All Preferred Terms
Other search criteria	Case Seriousness: Serious‡ Country Derived: USA

* See **Appendix A** for a description of the FAERS database.
† U.S. approval date for Myrbetriq.
‡ 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

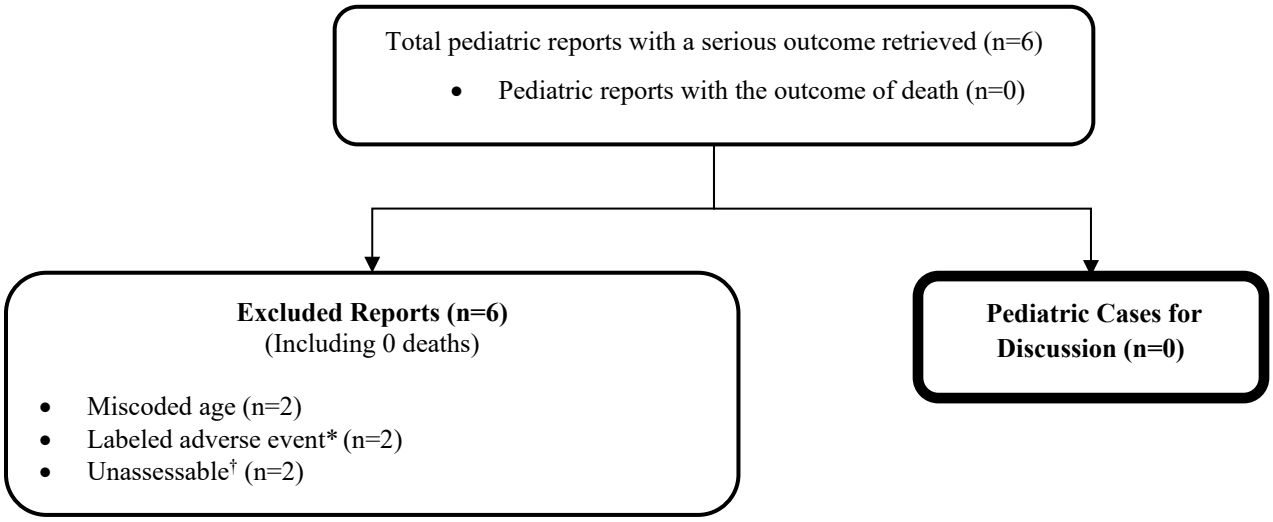
3 RESULTS

3.1 FAERS

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

Our FAERS search retrieved six U.S. serious pediatric reports for patients less than 18 years old from June 28, 2012, through February 12, 2025. We reviewed all U.S. FAERS pediatric reports with a serious outcome. We excluded all six reports from the case series for the reasons listed in **Figure 1**.

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



* 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 mirabegron in pediatric patients less than 18 years of age from June 28, 2012, through February 12, 2025, and identified 6 reports; however, all reports were excluded from further discussion because they did not refer to a pediatric patient, described labeled adverse events, or did not contain suffient information to assess causality.

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

5 CONCLUSION

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

6 REFERENCES

1. Myrbetriq/Myrbetriq granules (mirabegron) [package insert]. Astellas Pharma Global Development, Inc. Northbrook, IL. March 2021.

7 APPENDIX

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM

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.