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:	October 24, 2023
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Product Name:	Vesicare LS (solifenacin succinate) oral suspension
Pediatric Labeling Approval Date:	May 26, 2020
Application Type/Number:	NDA 209529
Applicant:	Astellas Pharma U.S., Inc.
TTT Record ID:	2023-5997

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Vesicare LS (solifenacin succinate) oral suspension 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 serious unlabeled adverse events associated with solifenacin succinate in pediatric patients.

Vesicare LS (solifenacin succinate) oral suspension is a muscarinic antagonist that was initially approved in the U.S. on May 26, 2020. Vesicare LS oral suspension is currently indicated for the treatment of neurogenic detrusor overactivity in pediatric patients aged 2 years and older. Solifenacin succinate is also available as Vesicare tablets for oral use (NDA 021518). Vesicare tablets was first approved on November 19, 2004, but is not indicated for use in the pediatric population.

This pediatric postmarketing safety review was prompted by pediatric labeling at original approval for Vesicare LS on May 26, 2020, which included the indication for pediatric patients aged 2 years and older. The safety and effectiveness of solifenacin succinate have not been established for pediatric patients younger than 2 years of age. A pediatric safety review for solifenacin succinate has not previously been presented to the Pediatric Advisory Committee.

DPV reviewed all serious FAERS reports with solifenacin succinate in pediatric patients less than 18 years of age from May 26, 2020 – July 31, 2023, and identified four reports; however, all reports were excluded from further discussion.

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

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Vesicare LS (solifenacin succinate) oral suspension 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 serious unlabeled adverse events associated with solifenacin succinate in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Vesicare LS (solifenacin succinate) oral suspension is a muscarinic antagonist that was initially approved in the U.S. on May 26, 2020. Vesicare LS oral suspension is currently indicated for the treatment of neurogenic detrusor overactivity in pediatric patients aged 2 years and older.[1] Solifenacin succinate is also available as Vesicare tablets for oral use (NDA 021518). Vesicare tablets was first approved on November 19, 2004, but is not indicated for use in the pediatric population.[2]

This pediatric postmarketing safety review was prompted by pediatric labeling at original approval for Vesicare LS on May 26, 2020, which included the indication for pediatric patients aged 2 years and older. The safety and effectiveness of solifenacin succinate have not been established for pediatric patients younger than 2 years of age.[1] A pediatric safety review for solifenacin succinate has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

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

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

- Gastric retention. (4, 5.3)
- Uncontrolled narrow-angle glaucoma. (4, 5.5)
- Hypersensitivity to this product or any of its components. (4, 5.1, 6.2)

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

- Angioedema and Anaphylactic Reactions: Promptly discontinue VESIcare LS and provide appropriate therapy. (5.1)
- Urinary Retention: VESIcare LS is not recommended for use in patients with clinically significant bladder outlet obstruction in the absence of clean intermittent catherization. (5.2)
- Gastrointestinal Disorders: VESIcare LS is not recommended for use in patients with decreased gastrointestinal motility. (5.3)
- Central Nervous System Effects: Somnolence has been reported with solifenacin succinate. Advise patients not to drive or operate heavy machinery until they know how VESIcare LS affects them. (5.4)
- Controlled Narrow-Angle Glaucoma: Use VESIcare LS with caution in patients being treated for narrow-angle glaucoma. (5.5)
- QT Prolongation in Patients at High Risk of QT Prolongation: VESIcare LS is not recommended for use in patients at high risk of QT prolongation, including patients with a known history of QT prolongation and patients taking medications known to prolong the QT interval. (5.6)

---------- ADVERSE REACTIONS ----------
The most common adverse reactions (> 2%) were constipation, dry mouth and urinary tract infection. (6.1)

8.4 Pediatric Use
The safety and effectiveness of VESIcare LS have been established in pediatric patients aged 2 years and older for the treatment of neurogenic detrusor overactivity (NDO) and the information on this use is discussed throughout the labeling. The safety and effectiveness of VESIcare LS have not been established in pediatric patients less than 2 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	August 9, 2023
Time period of search	May 26, 2020† - July 31, 2023
Search type	RxLogix Post-Market Cases
Product terms	Product Active Ingredient: Solifenacin succinate
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. † Vesicare LS U.S. approval date Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities	

3 RESULTS

3.1 FAERS

3.1.1 Total Number of FAERS Reports by Age

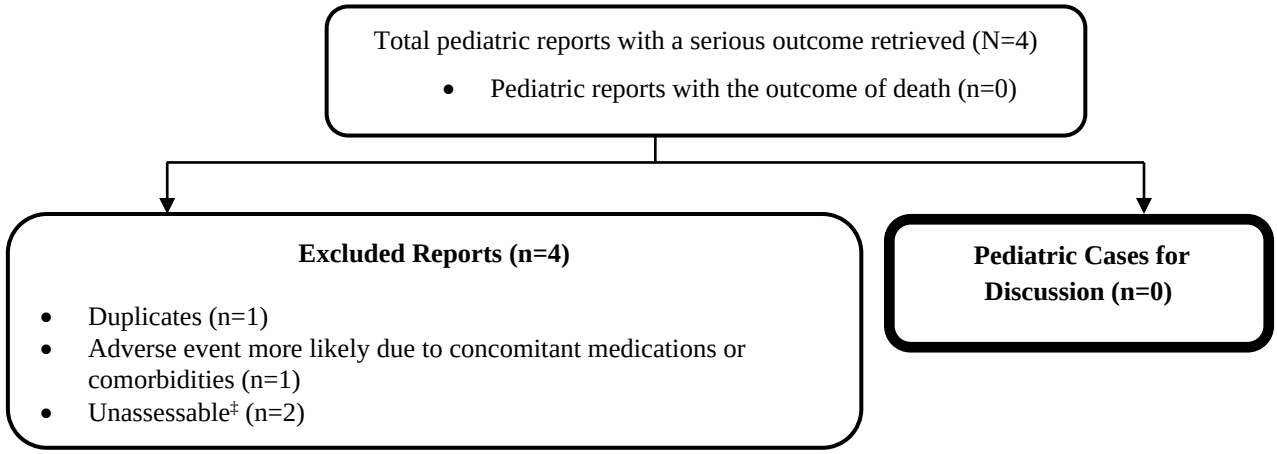
Table 2 presents the number of adult and pediatric FAERS reports from May 26, 2020 – July 31, 2023, with solifenacin succinate.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From May 26, 2020 – July 31, 2023, With Solifenacin Succinate			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 18 years)	380 (127)	273 (29)	9 (3)
Pediatrics (0 - < 18 years)	6 (1)	4 (0)	0‡ (0)
* May include duplicates and transplacental exposures, and have not been assessed for causality † 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.			

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved four serious pediatric reports from May 26, 2020 – July 31, 2023. We reviewed all 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** presents the selection of cases for the pediatric case series.

Figure 1. Selection of Serious Pediatric Cases With Solifenacin Succinate



* 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.

3.1.3 Summary of Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.4 Summary of Serious Non-Fatal Pediatric Cases (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all serious FAERS reports with solifenacin succinate in pediatric patients less than 18 years of age from May 26, 2020 – July 31, 2023, and identified four reports; however, all reports were excluded from further discussion.

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

5 CONCLUSION

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

6 REFERENCES

1. Vesicare LS (solifenacin succinate) oral suspension [Prescribing information]. Northbrook, IL; Astellas Pharmac U.S., Inc.: May, 2020.

2. Vesicare (solifenacin succinate) tablets, for oral use [Prescribing information]. Northbrook, IL; Astellas Pharmac U.S., Inc.: May, 2020.

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.

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