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:	December 19, 2024
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Product Names:	Fiasp (insulin aspart) solution; intravenous, subcutaneous Fiasp Flextouch (insulin aspart) solution; subcutaneous Fiasp Penfill (insulin aspart) solution; subcutaneous
Pediatric Labeling Approval Date:	December 19, 2019
Application Type/Number:	BLA 208751
Applicant:	Novo Nordisk, Inc.
TTT Record ID:	2024-10787

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Fiasp (insulin aspart) solution 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 Fiasp in pediatric patients.

Fiasp is a rapid-acting human insulin analog initially approved in the U.S. on September 29, 2017, and is currently indicated to improve glycemic control in adult and pediatric patients with diabetes mellitus.

This pediatric postmarketing safety review was stimulated by pediatric labeling for Fiasp on December 19, 2019, which expanded the indication to include glycemic control and continuous subcutaneous insulin infusion use in pediatric patients.

DPV reviewed all U.S. serious FAERS reports with Fiasp in pediatric patients less than 18 years of age from September 29, 2017, through September 3, 2024, and identified six 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 Fiasp in pediatric patients less than 18 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Fiasp (insulin aspart) solution 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 Fiasp in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Fiasp (insulin aspart) solution is a rapid-acting human insulin analog initially approved in the U.S. on September 29, 2017, and is currently indicated to improve glycemic control in adult and pediatric patients with diabetes mellitus. Fiasp is available in the following dosage forms: multiple-dose vial, FlexTouch pen, PenFill cartridge, and PumpCart cartridge.[1]

This pediatric postmarketing safety review was stimulated by pediatric labeling for Fiasp on December 19, 2019, which expanded the indication to include glycemic control and continuous subcutaneous insulin infusion use in pediatric patients.

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

1.2 RELEVANT LABELED SAFETY INFORMATION

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

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

- During episodes of hypoglycemia.
- Hypersensitivity to insulin aspart or any of the excipients in FIASP.

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

- *Never share* a FIASP FlexTouch pen, PenFill cartridge or PenFill cartridge device between patients, even if the needle is changed.
- *Hyperglycemia or hypoglycemia with changes in insulin regimen*: Make changes to a patient's insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) under close medical supervision with increased frequency of blood glucose monitoring.
- *Hypoglycemia*: May be life-threatening. Increase frequency of glucose monitoring with changes to: insulin dosage, co-administered glucose lowering medications, meal pattern, physical activity; and in patients with renal impairment or hepatic impairment or hypoglycemia unawareness.
- *Hypoglycemia due to medication errors*: Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection.

- *Hypokalemia*: May be life-threatening. Monitor potassium levels in patients at risk for hypokalemia and treat if indicated.
- *Hypersensitivity reactions*: Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Discontinue FIASP, monitor and treat if indicated.
- *Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs)*: Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs.
- *Hyperglycemia and Ketoacidosis Due to Insulin Pump Device Malfunction:* Monitor glucose and administer FIASP by subcutaneous injection if pump malfunction occurs.

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

Adverse reactions observed with FIASP include: hypoglycemia, allergic reactions, hypersensitivity, injection/infusion site reactions, lipodystrophy, and weight gain.

----------USE IN SPECIFIC POPULATIONS----------

8.4 Pediatric Use

The safety and effectiveness of FIASP have been established to improve glycemic control in pediatric patients with diabetes mellitus. Use of FIASP for this indication is supported by evidence from an adequate and well-controlled study in 777 pediatric patients with type 1 diabetes mellitus aged 2 to 17 years, and from studies in adults with diabetes mellitus.

Pediatric patients with type 1 diabetes mellitus treated with mealtime and postmeal FIASP reported a higher rate of blood glucose confirmed hypoglycemic episodes compared to patients treated with NovoLog; the imbalance was greater during the nocturnal period. Monitor blood glucose levels closely in pediatric patients.

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	September 4, 2024
Time period of search	September 29, 2017† - September 3, 2024
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product name: Fiasp Case Application Number: BLA 208751
MedDRA search terms (Version 27.0)	All Preferred Terms
Other search terms‡	Case Seriousness: Serious

Table 1. FAERS Search Strategy*
* See Appendix A for a description of the FAERS database. † U.S. approval date for Fiasp (insulin aspart) solution ‡ 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. Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities

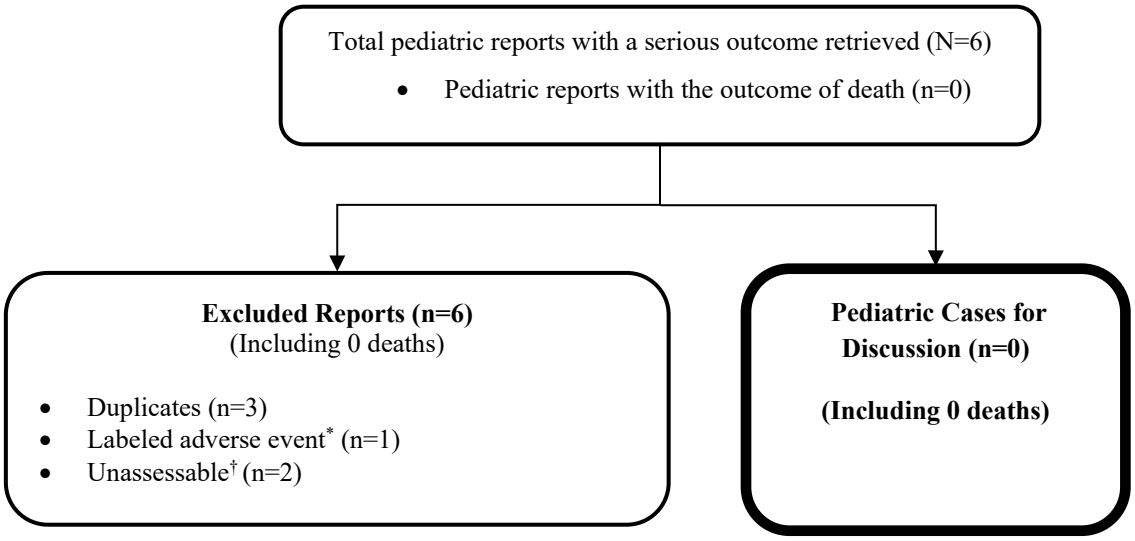
3 RESULTS

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 September 29, 2017, through September 3, 2024. 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 Fiasp



* 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 Fiasp in pediatric patients less than 18 years of age from September 29, 2017, through September 3, 2024, and identified six 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 Fiasp in pediatric patients less than 18 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Fiasp (insulin aspart) [package insert]. Plainsboro, NJ. Novo Nordisk, Inc. 2023.

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.