Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Pediatric Postmarketing Pharmacovigilance and Drug Utilization Review

Date:	December 22, 2016
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Product Name:	Jetrea® (ocriplasmin) Intravitreal Injection
Pediatric Labeling Approval Date:	June 13, 2014
Application Type/Number:	BLA 125422
Applicant/Sponsor:	ThromboGenics, Inc.
OSE RCM #:	2016-2162

EXECUTIVE SUMMARY

In accordance with the Food and Drug Administration Amendments Act (FDAAA) Best Pharmaceuticals for Children Act (BPCA) and Pediatric Research Equity Act (PREA), the Office of Surveillance and Epidemiology (OSE) evaluated postmarketing adverse event reports with a serious outcome for Jetrea® (ocriplasmin) Intravitreal Injection in pediatric patients.

Jetrea® (ocriplasmin) Intravitreal Injection was first approved in 2012 and is indicated for the treatment of symptomatic vitreomacular adhesion. Ocriplasmin was not approved for a pediatric indication.

There are currently no cases in the FDA Adverse Event Reporting System (FAERS) in pediatric patients for ocriplasmin. However, the Division of Pharmacovigilance will continue routine pharmacovigilance monitoring of the FAERS database for cases reported in the pediatric population.

1 INTRODUCTION

1.1 PEDIATRIC REGULATORY HISTORY

Jetrea® (ocriplasmin) is available as a single-use glass vial containing ocriplasmin 0.5 mg in 0.2 mL solution for intravitreal injection (2.5 mg/mL). It is indicated for the treatment of symptomatic vitreomacular adhesion.

Pediatric Labeling Date: June 13, 2014

Label Changes Summary: The use of Jetrea in pediatric patients is not recommended. A single center, randomized, placebo controlled, double masked clinical study to investigate the safety and efficacy of a single intravitreal injection of 0.175 mg ocriplasmin in pediatric subjects as an adjunct to vitrectomy was conducted in 24 eyes of 22 patients. There were no statistical or clinical differences between groups for the induction of total macular PVD, any of the secondary endpoints or adverse events.

1.2 HIGHLIGHTS OF LABELED SAFETY ISSUES

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

None.

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

- Decreases in vision due to progression of the condition with traction may occur requiring surgical intervention. Patients should be monitored and instructed to report any symptoms without delay.
- Intravitreal injection procedure associated effects (intraocular inflammation/infection, intraocular hemorrhage and increased IOP) may occur following an intravitreal injection. Patients should be monitored and instructed to report any symptoms without delay.
- Potential for lens subluxation.

----------ADVERSE RECTIONS----------

- The most commonly reported reactions (≥ 5%) in patients treated with JETREA were vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment, and retinal edema.

2 POSTMARKET ADVERSE EVENT REPORTS

2.1 METHODS AND MATERIALS

2.1.1 FDA Adverse Event Reporting System (FAERS) Search Strategy

DPV searched the FAERS database with the strategy described in Table 2.1.1. See Appendix A for a description of the FAERS database.

Table 2.1.1 FAERS Search Strategy

Date of Search	November 14, 2016
Time Period of Search	Entire database as of November 14, 2016
Search Type	FBIS Product-Manufacturer Reporting Summary
Product Name(s)	Ocriplasmin (Product Active Ingredient)
Search Parameters	All ages, all outcomes, worldwide

2.2 RESULTS

2.2.1 Total number of FAERS reports by Age

Table 2.2.1 Total Adult and pediatric FAERS reports* as of November 14, 2016 with Jetrea® (ocriplasmin) Intravitreal Injection, 2.5 mg/mL

	All reports (US)	Serious† (US)	Death (US)
Adults (≥ 17 years)	235 (158)	190 (113)	1 (1)
Pediatrics (0 - <17 years)	0 (0)	0 (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, and other serious important medical events.***

‡ 0 reports of pediatric deaths were identified among reports not reporting an age.

3 DISCUSSION

There were no reports for ocriplasmin in pediatric patients, and, therefore, no safety signals were identified.

4 CONCLUSION

There is no evidence from these data that there are pediatric safety concerns with this drug at this time.

5 RECOMMENDATIONS

The Division of Pharmacovigilance will continue routine pharmacovigilance monitoring of the FAERS database for cases reported in the pediatric population.

6 APPENDICES

6.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

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 the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary (FPD).

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 or not 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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