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Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

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Product Name:	Xeglyze (abametapir)
Pediatric Labeling Approval Date:	July 24, 2020
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Applicant:	Hatchtech Pty, Ltd
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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xeglyze lotion (abametapir) in pediatric patients less than 17 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with abametapir in pediatric patients.

Xeglyze (abametapir) is a pediculicide initially approved in the United States on July 24, 2020. Abametapir is currently indicated for the topical treatment of head lice infestation in patients 6 months of age and older. Abametapir should be used in the context of an overall lice management program.

This pediatric postmarketing safety review was prompted by the pediatric labeling at original approval for abametapir which included an indication for pediatric patients aged 6 months and older. Abametapir has not been previously presented before the Pediatric Advisory Committee.

DPV searched FAERS for all serious reports with abametapir in pediatric patients less than 17 years of age through February 22, 2024, and did not identify any reports.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with abametapir in pediatric patients less than 17 years of age.

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

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Xeglyze (abametapir) lotion in pediatric patients less than 17 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with abametapir in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Xeglyze (abametapir) is a pediculicide initially approved in the United States on July 24, 2020. Abametapir is currently indicated for the topical treatment of head lice infestation in patients 6 months of age and older. Abametapir should be used in the context of an overall lice management program.[1]

This pediatric postmarketing safety review was prompted by the pediatric labeling at original approval for abametapir, which included an indication for pediatric patients aged 6 months and older.[2] Of note, the Applicant for abametapir has never marketed the product in the United States.[3] Abametapir has not been previously presented before the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The abametapir labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional abametapir labeling information, please refer to the full prescribing information.[4]

---------- CONTRAINDICATIONS ----------
None.

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

- Risk of Neonatal Benzyl Alcohol Toxicity: Systemic exposure to benzyl alcohol has been associated with serious adverse reactions and death in neonates and low birth-weight infants. Safety and effectiveness in pediatric patients below the age of 6 months have not been established. Use is not recommended in pediatric patients under 6 months of age because of the potential for increased systemic absorption. (5.1)
- Risk of Benzyl Alcohol Toxicity from Accidental Ingestion: Administer only under direct supervision of an adult. (5.2)

---------- ADVERSE REACTIONS ----------
Most common adverse reactions (incidence of ≥ 1%) were erythema, rash, skin burning sensation, contact dermatitis, vomiting, eye irritation, pruritus, and hair color changes. (6.1)

8.4 Pediatric Use

The safety and effectiveness of XEGLYZE have been established in pediatric patients 6 months of age and older [see Clinical Pharmacology (12) and Clinical Studies (14)].

The safety and effectiveness of XEGLYZE have not been established in pediatric patients below the age of 6 months. XEGLYZE is not recommended in pediatric patients under 6 months of age because of the potential for increased systemic absorption due to a high ratio of skin surface to body mass and the potential for an immature skin barrier.

XEGLYZE contains benzyl alcohol. Benzyl alcohol has been associated with serious adverse reactions and death in neonates and low birth-weight infants. The “gasping syndrome” (characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine) has been associated

with intravenously administered benzyl alcohol dosages >99 mg/kg/day in neonates and low birthweight infants. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse.

The minimum amount of benzyl alcohol at which toxicity may occur is not known. Premature and low-birthweight infants, as well as patients receiving high dosages, may be more likely to develop toxicity [see Warnings and Precautions (5.1)].

Because of the risk of accidental ingestion, XEGLYZE should be administered to pediatric patients only under direct adult supervision [see Warnings and Precautions (5.2)].

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 23, 2024
Time period of search	All dates through February 22, 2024
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product Active Ingredient: Abametapir
MedDRA search terms (Version 26.1)	All Preferred Terms
* See Appendix A for a description of the FAERS database. 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 through February 22, 2024, with abametapir.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA Through February 22, 2024, With Abametapir			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 17 years)	0 (0)	0 (0)	0 (0)
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, or other serious important medical events.			

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved no pediatric reports through February 22, 2024.

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 searched FAERS for all serious reports with abametapir in pediatric patients less than 17 years of age through February 22, 2024, and did not identify any reports.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with abametapir in pediatric patients less than 17 years of age.

5 CONCLUSION

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

6 REFERENCES

1. Xeglyze (abametapir) lotion. [Prescribing information]. Princeton, NJ; Dr. Reddy's Laboratories, Inc.: June, 2020.
2. Approval Letter. NDA 206966. July 24, 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/206966Orig1s000ltr.pdf
3. Orange Book. NDA 206966. Available at: https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=206966#20157
4. Xeglyze (abametapir) lotion [Prescribing information]. Princeton, NJ; Dr. Reddy's Laboratories, Inc.: January, 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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