

**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 Review**

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**Product Name:** Xerese® (5% acyclovir and 1% hydrocortisone cream)

**Pediatric Labeling  
Approval Date:** January 22, 2014

**Application Type/Number:** NDA 022436

**Applicant/Sponsor:** Valeant

**OSE RCM #:** 2016-1648

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## **EXECUTIVE SUMMARY**

In accordance with the Pediatric Research Equity Act (PREA), the Office of Surveillance and Epidemiology (OSE) evaluated postmarketing adverse event reports for Xerese® in pediatric patients.

Xerese® is a topical cream which consists of a combination of acyclovir, a herpes simplex virus nucleoside analog DNA polymerase inhibitor, and hydrocortisone, a corticosteroid. Xerese® was first approved in 2009, and it is currently indicated for the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and children (6 years of age and older).

The FDA Adverse Event Reporting System (FAERS) database was searched for all reports of adverse events (serious and non-serious) from August 31, 2011 through July 31, 2016 with Xerese®. FAERS contained no pediatric reports for Xerese®. Based on current FAERS data, there is no evidence that there are new pediatric safety concerns with Xerese® at this time. DPV recommends routine pharmacovigilance monitoring.

# 1 INTRODUCTION

## 1.1 PEDIATRIC REGULATORY HISTORY<sup>1,2</sup>

Xerese<sup>®</sup> is a topical cream which consists of a combination of acyclovir, a herpes simplex virus nucleoside analog DNA polymerase inhibitor, and hydrocortisone, a corticosteroid. Each gram of Xerese<sup>®</sup> contains 5% (w/w) acyclovir and 1% (w/w) hydrocortisone in an aqueous cream base. Xerese<sup>®</sup> is applied topically five times per day for five days; therapy should be initiated as early as possible after the first signs and symptoms (i.e., during the prodrome or when lesions appear).

Xerese<sup>®</sup> was initially approved in 2009 for the early treatment of signs and symptoms of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores in adults and adolescents 12 years of age and older. For the January 2012 Pediatric Advisory Committee (PAC) meeting, DPV searched the Adverse Event Reporting System (AERS) database for all reports of adverse events (serious and non-serious) from the date of initial FDA approval (July 31, 2009) through August 30, 2011. AERS contained no reports for Xerese<sup>®</sup> and no new pediatric safety concerns were identified.

In 2014, the indication for Xerese<sup>®</sup> was expanded to include 6 years to less than 12 years of age. This was based on the results of an open-label, multi-center, phase 3 study of Xerese<sup>®</sup> in the treatment of recurrent herpes labialis in children 6 to 11 years of age (Study MP800; n=54). No primary efficacy variables were evaluated in this study as it was designed to collect safety data. Overall, adverse events (all grades, all causality) were reported among 8 (14.8%) subjects receiving Xerese<sup>®</sup>. Most adverse events were mild and most were considered by study investigators as unrelated to study treatment, and no new safety signals were identified. The overall safety profile of Xerese<sup>®</sup> in children ages 6 to 11 years of age appears similar to that previously described for adults and adolescents.

DPV has not completed any further pediatric reviews for Xerese<sup>®</sup>. To our knowledge, there is no pending regulatory action involving new safety information for this drug in the pediatric population.

## 1.2 HIGHLIGHTS OF LABELED SAFETY ISSUES

The Xerese<sup>®</sup> (acyclovir and hydrocortisone) label includes the following information:

### CONTRAINDICATIONS

- None

### WARNINGS AND PRECAUTIONS

- Only for topical use for recurrent herpes labialis on the lips and around the mouth.

### ADVERSE REACTIONS

- The following most common adverse reactions (< 1%) were local skin reactions:

- Drying or flaking of the skin; burning or tingling; erythema; pigmentation changes; application site reactions including signs and symptoms of inflammation.

## 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	August 9, 2016
Time Period of Search	August 31, 2011* - July 31, 2016
Search Type	FAERS Business Intelligence Solution (FBIS) Profile Query Product-Manufacturer Reporting Summary
Product Names	Product Name: Xerese Product Active Ingredient: Acyclovir/Hydrocortisone NDA: 022436
Search Parameters	All ages, all outcomes, worldwide

*\* This review serves as an update to the previous review for the January 2012 PAC Meeting*

### 2.2 RESULTS

#### 2.2.1 Total number of FAERS reports by Age

**Table 2.2.1 Total Adult and pediatric FAERS reports\* from August 31, 2011 through July 31, 2016 with Xerese®**

	All reports (US)	Serious <sup>†</sup> (US)	Death (US)
<b>Adults (&gt; 17 years)</b>	2 (2)	1 (1)	0 (0)
<b>Pediatrics (0 - &lt;17 years)</b>	0 (0)	<b>0 (0)</b>	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.*

FAERS contained no pediatric reports for Xerese®.

## 3 DISCUSSION

There were no new safety signals or deaths identified in this review.

#### **4 CONCLUSION**

There is no evidence from these data that there are new pediatric safety concerns with Xerese<sup>®</sup> at this time.

#### **5 RECOMMENDATIONS**

DPV will continue routine pharmacovigilance monitoring for Xerese<sup>®</sup>.

#### **6 REFERENCES**

- 1) Development Resources for Medical, Statistical, and Clinical Pharmacology Reviews of Pediatric Studies Conducted under Section 505A and 505B of the Federal Food, Drug, and Cosmetic Act, as amended by the FDA Safety and Innovation Act of 2012 (FDASIA). Available at:  
<http://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/ucm316937.htm>. Accessed: August 2016.
- 2) Xerese<sup>®</sup> (5% acyclovir and 1% hydrocortisone cream), NDA 022436 - Approved Product Label. Available at:  
[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/022436s004lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/022436s004lbl.pdf). Accessed: August 2016.

## 7 APPENDICES

### 7.1 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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/s/  
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