CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206966Orig1s000

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Division of Risk Management (DRM)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Application Type	NDA
Application Number	206966
PDUFA Goal Date	May 12, 2020
OSE RCM #	2016-1233
Reviewer Name(s)	Bob Pratt, PharmD
Team Leader	Donella Fitzgerald, PharmD
Deputy Division Director	Jamie Wilkins, PharmD
Review Completion Date	February 10, 2020
Subject	Memorandum to File
Established Name	Abametapir
Trade Name	Xeglyze
Name of Applicant	Dr. Reddy's Laboratories, Inc.
Therapeutic Class	Metalloproteinase inhibitor
Formulation(s)	Lotion, 0.74%
Dosing Regimen	Apply to dry hair and scalp for 10 minutes and then rinse off with water

1 Introduction

This memorandum by the Division of Risk Management (DRM) pertains to New Drug Application (NDA) 206966 for Xeglyze (abametapir) originally submitted on September 14, 2015 by Hatchtech Pty Ltd.[a] The proposed indication is for the treatment of head lice infestation in patients 6 months of age and older. DRM completed a review of the application on June 13, 2016 and concluded that, based on the benefit-risk profile, a REMS is not necessary.[1] A Complete Response Letter for the NDA was issued by the Agency on August 30, 2016 due to deficiencies identified during inspection of the manufacturing facility. The NDA was resubmitted on November 12, 2019 in response to the deficiencies. The Applicant did not submit a proposed REMS or risk management plan with the application. This NDA is under review in the Division of Dermatology and Dental Products (DDDP).

2 Background

2.1 Product Information

Xelgyze (abametapir), a new molecular entity (NME), is a metalloproteinase inhibitor that interrupts a number of physiological processes in insects, including nutrition and other cellular developmental processes critical to egg development and survival of crawling lice.[2] The proposed indication is for the treatment of head lice infestation in patients 6 months of age and older. Abametapir is to be supplied as a 0.74% topical lotion to be applied once to the scalp and dry hair for 10 minutes and then rinsed off with water. Abametapir is not currently approved in any other jurisdiction.

2.2 Regulatory History

The following is a summary of the regulatory history for NDA 206966 relevant to this review:

- 9/14/2015: NDA 206966 submission for the treatment of head lice infestation in patients 6 months of age and older.
- 8/30/2016: Complete Response Letter issued by the Agency due to manufacturing facility deficiencies.
- 11/12/2019: Resubmission of NDA 206966 as a complete response to the deficiencies. The Applicant's response proposes the use of an alternative manufacturing site for the drug substance. The Applicant states no additional nonclinical and clinical studies have been conducted after submission of the NDA; in addition, no additional patients have been exposed to the drug product under any other means.

3 Discussion of Need for a REMS

The efficacy of abametapir was convincingly demonstrated in two adequate and well-controlled Phase 3 clinical trials under conditions of actual use. Adverse reactions that occurred in at least 1% of patients in the abametapir group and at a greater frequency than in the vehicle group included erythema (4%), rash

[a] Ownership of the NDA was transferred from Hatchtech Pty Ltd to Dr. Reddy's Laboratories effective December 29, 2015.

(3.2%), skin burning sensation (2.6%), contact dermatitis (1.7%), vomiting (1.7%), eye irritation (1.2%), and hair color changes (1%). These adverse reactions were all mild to moderate in severity and reversible.[3] DRM evaluated the risks of abametapir in a review dated June 13, 2016 and determined that a REMS is not necessary to ensure the benefits outweigh the risks of abametapir; no major safety signals have been identified and the drug's safety profile appears to be similar to or have less of a risk for serious adverse events than what is reported for other approved treatments for head lice infestation.[4] The Applicant has indicated no additional nonclinical and clinical studies have been conducted after submission of the NDA, and that no additional patients have been exposed to the drug product under any other means. Hence, there are no updated safety data to evaluate. Therefore, at the time of this memorandum, the safety profile of abametapir has not changed.

4 Conclusion and Recommendations

Based on the analysis detailed in the initial REMS review, and the absence of new safety data that changes the benefit-risk profile, we maintain our determination that a REMS is not necessary to ensure the benefits of abametapir outweigh its risks.

Should DDDP have any concerns or questions or if new safety information becomes available, please send a consult to DRM.

5 Appendices

5.1 References

[1] Hachey E. Division of Risk Management, REMS Review, NDA 206966, June 13, 2016.
[2] Ibid
[3] Marcus K. Division of Dermatology and Dental Products, Division Director Summary Review for Regulatory Action, NDA 206966, August 24, 2016.
[4] See endnote 1.

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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 Medication Error Prevention and Risk Management

Risk Evaluation and Mitigation Strategy (REMS) Review

Date:	June 13, 2016
Reviewer(s):	Erin Hachey, PharmD, Division of Risk Management (DRISK)
Team Leader:	Jamie Wilkins Parker, PharmD, DRISK
Acting Deputy Director:	Kellie Taylor, PharmD, MPH, DRISK
Subject:	Evaluation to determine if a REMS is necessary
Drug Name(s):	Xeglyze (abametapir)
Therapeutic Class:	Pediculicide, metalloproteinase inhibitor
Formulation:	Lotion, 0.74%
Dosing Regimen: content of one the hair and	Apply Xeglyze Lotion to dry hair in an amount (up to the full bottle) sufficient to thoroughly coat the hair and scalp. Leave on scalp for 10 minutes and then rinse off with warm water
Proposed Indication(s): older	Treatment of head lice infestation in patients 6 months of age and
Application Type/Number:	NDA 206966
Applicant/Sponsor:	Dr. Reddy's Laboratories, SA
OSE RCM #:	2016-1233

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1 Introduction

This review by the Division of Risk Management (DRISK) evaluates whether a risk evaluation and mitigation strategy (REMS) is necessary for the new molecular entity (NME) Xeglyze (abametapir), to ensure the benefits outweigh the risks. A new drug application (NDA 206966) for Xeglyze 0.74% lotion was received by the Division of Dermatology and Dental Products (DDDP) from Hatchtech Pty Ltd (Hatchtech) on September 14, 2015. The Applicant did not submit a REMS or risk management plan with the application. There was a change in ownership of the NDA from Hatchtech to Dr. Reddy's Laboratories, SA on December 30, 2015.

2 Background

2.1 Product Information

The new molecular entity (NME) abametapir is the active moiety in Xeglyze lotion, which is intended as a single-application topical therapy for head lice infestation. Xeglyze is a pediculicide that achieves its therapeutic activity by coordinating as a chelating ligand to form complexes with transition metal ions. Through this means, Xeglyze acts as a metalloproteinase inhibitor, interrupting a number of physiological processes in insects, including nutrition and other cellular developmental processes critical to egg development and survival of crawling lice. The proposed indication of Xeglyze is for the topical treatment of head lice infestation ((b) (4) in patients 6 months of age and older.

The proposed dosage form of Xeglyze is a topical lotion containing 0.74% abametapir, supplied in a 200 g bottle with a child-resistant closure. The proposed recommended dosing regimen is a single application to dry hair in an amount (up to the full content of one bottle) sufficient to thoroughly coat the hair and scalp, to be left on the hair and scalp for 10 minutes, then rinsed off with warm water. [1] Patients should be advised to avoid exposure to (b) (4) eyes, (b) (4)

The Applicant's proposed mechanism of action of Xeglyze, acting on both the louse and the egg, differs from other FDA-approved head lice therapies currently marketed in the U.S. that target ion channels of the nerve or muscle, to result in hyperexcitation, paralysis, and subsequent death of the insect, or inhibit lice from closing their respiratory spiracles, allowing the vehicle to obstruct the spiracles, thereby causing the lice to asphyxiate. Xeglyze's mechanism of action is

[1] Clark K L. DDDP, Clinical Review of Xeglyze Lotion, dated April 27, 2016.

unique as, to date, no currently marketed FDA-approved product has data to support ovicidal activity.[2]

Xeglyze lotion is currently not marketed outside of the U.S.

2.2 Regulatory History

The following is a summary of the regulatory history for NDA 206966 relevant to this review:

- September 14, 2015: The Agency received an original NDA submission from Hatchtech for Xeglyze 0.74% lotion. The Applicant did not submit a proposed REMS.
- December 30, 2015: The Applicant notified the Agency of the change in ownership of the application from Hatchtech to Dr. Reddy's Laboratories, SA, effective December 29, 2015 (Seq. 0004).
- January 20, 2016: The 120-day Safety Update was submitted to the Agency (Seq. 0006).
- February 8, 2016: The Mid-Cycle Meeting was held between the Agency and the Applicant via teleconference. The Agency informed the Applicant that, based on the currently available data, there were no safety issues that would require a REMS for Xeglyze.
- May 20, 2016: The Late-Cycle Meeting was held between the Agency and the Applicant. A REMS was not discussed with the Applicant.

3 Medical Condition and Treatment Options

3.1 Description of the Medical Condition

Head lice infestation (*Pediculus humanus capitis*) is a common problem, affecting 6 to 12 million people per year, according to the Centers for Disease Control and Prevention, most commonly children aged 3 to 11 years. Although not severe or life-threatening, head lice infestation is a significant cause of lost school and work days for affected children and their caregivers. There are multiple drugs approved for the treatment of head lice infestation. However, resistance to the available over-the-counter pediculicides has been reported. A new product, with ovicidal activity, requiring only a single treatment, with a favorable safety and efficacy profile would be a useful addition to currently available treatments.[3]

[2] Hatchtech. Clinical Overview for Xeglyze, received September 14, 2015.

[3] Clark K L. DDDP. Clinical Review of Xeglyze Lotion, dated April 27, 2016.

The adult head louse is 2-3 mm long, has 6 legs, and is tan to grayish-white in color. The female lives up to 4 weeks and, once mature, can lay up to 10 eggs per day. The tiny eggs are firmly attached to the base of the hair shaft with a glue-like substance produced by the louse. The eggs are incubated by body heat and typically hatch in 8 to 9 days. Once it hatches, a nymph passes through 3 stages to reach adulthood in approximately 12 days. The female louse can mate and begin to lay viable eggs approximately 1.5 days after becoming an adult. If not treated, the cycle repeats itself approximately every 3 weeks. To feed, the louse injects its saliva, which has vasodilatory and anticoagulation properties, into the scalp of its host, which helps the louse suck blood every few hours. The host develops sensitization to components of the saliva, which leads to pruritis.[4]

3.2 Description of Current Treatment Options

The goal of therapy is to eradicate lice in the adult and nymph stages, and to remove nits from the patient's hair. Treatment for head lice is recommended for persons diagnosed with an active infestation. All household members and other close contacts should be checked; those persons with evidence of an active infestation should be treated, and many experts believe their bedmates should be prophylactically treated at the same time. For pediculicides that are only weakly ovicidal or not ovicidal, routine re-treatment is recommended. For those that have stronger ovicidal activity, re-treatment is recommended only if live lice are still present several days after treatment. The ideal treatment should be safe, effective, readily available, easy to use, and inexpensive. Local patterns of resistance (if known), and cost also are considerations when choosing a treatment choice.

No currently available pediculicide is 100% ovicidal, and resistance to pyrethrins, permethrin, and malathion has been reported. This resistance is not unanticipated, because insects develop resistance to products over time. The actual prevalence of resistance to particular products is not known and can be regional. For patients younger than 6 months of age, or if the caregiver cannot afford or does not wish to use a pediculicide, manual removal via wet combing or an occlusive method can be used, with emphasis on careful technique and the use of 2 to 4 properly timed treatment cycles.[5]

Sklice, Natroba, and Ulesfia are all approved for the treatment of head lice in patients 6 months of age and older. Of these three products, only Sklice is intended as a single application dosage regimen. Another treatment option, Lindane shampoo, although effective, carries a boxed

[4] Devore, C. D., Schutze, G. E., Okamoto, J., Allison, M., Ancona, R., Attisha, E., ... & Minier, M. (2015). Head Lice. Pediatrics, 135(5), e1355-e1365.

[5] Ibid.

warning for neurotoxicity, with reports of seizures and even death following repeat or prolonged application, and in rare cases, following a single application according to directions.

When treating head lice, supplemental measures (e.g. washing bedding, clothing, and towels of the infested person using the machine's hottest cycle) can be combined with recommended medicine (pharmacologic treatment); however, such additional (non-pharmacologic) measures generally are not required to eliminate a head lice infestation.

4 Benefit Assessment

4.1 Efficacy of Xeglyze Lotion for the Treatment of Head Lice Infestation

The efficacy and safety of Xeglyze lotion for the treatment of head lice infestation were demonstrated in two Phase 3 pivotal trials (Ha03-001 and Ha03-002) in subjects 6 months of age and older with active head lice infestation. Both studies were randomized, double-blind, multi-center, vehicle-controlled, parallel-group, and conducted under actual-use conditions. The studies were conducted in 7 centers in the U.S., and well-distributed geographically, which is important because resistance to permethrin and pyrethroids has shown geographic variability in the U.S.

Both Trial Ha03-001 and Trial Ha03-002 had identical protocols. All members of a household who were 6 months of age and older were considered for enrollment. The index subject of each household was the youngest person within that household with at least 3 live lice present, as assessed at screening. Non-index household members were defined as the remaining members of the household with at least 1 live louse present at screening; these subjects were randomized to the same treatment group as the index subject. The Applicant's primary efficacy endpoint was the percent of index subjects lice-free at all follow-up visits through Day 14. The administration of the study product at home by the patient or caregiver represented actual-use conditions.

Two additional studies, Ha03-003 and Ha03-004, were open-label studies which evaluated the tolerability and safety of Xeglyze, including systemic benzyl alcohol exposure, in pediatric subjects aged 6 months to 17 years. No adjunctive measures (e.g. nit combing) were included in the study protocols. All subjects were required to return to the trial site for follow-up visits on Day 1, Day 7, and Day 14 for safety and efficacy assessments.

Trial Ha03-001

A total of 108 index subjects were randomized to receive Xeglyze (n= 53) or Vehicle (n= 55). The primary efficacy endpoint was the percent of index subjects lice-free at all follow-up visits (Days

1, 7, and 14). The proportion of index subjects achieving the primary endpoint were 81.1% (n= 43) and 50.9% (n= 28) for the Xeglyze and Vehicle groups, respectively (p = 0.001).

Trial Ha03-002

A total of 108 index subjects were randomized to receive Xeglyze (n= 55) or Vehicle (n= 53). The primary efficacy endpoint was the percent of index subjects lice-free at all follow-up visits (Days 1, 7, and 14). The proportion of index subjects achieving the primary endpoint were 81.8% (n= 45) and 47.2% (n= 25) for the Xeglyze and Vehicle groups, respectively (p < 0.001).

For both Phase 3 trials, the protocol-specified secondary endpoints were the proportion of index subjects who are lice-free at the Day 1 and Day 7 visits. However, these endpoints were determined not to be clinically relevant or meaningful, due to the life cycle of the head louse.

Trials Ha03-003 and Ha03-004

Trials Ha03-003 and Ha03-004 were multi-center, open-label studies to evaluate the safety and tolerability of Xeglyze in 60 pediatric subjects (age 6 months to 17 years). Additionally, these studies provided the data for systemic benzyl alcohol exposure in subjects administered Xeglyze. According to the Clinical Pharmacology reviewer, benzyl alcohol was measurable in the serum of 7 out of 39 evaluable subjects, and the Cmax of benzyl alcohol in these 7 subjects ranged from 0.52 to 3.57 µg/mL.

According to the Clinical reviewer, the data from the pivotal Phase 3 trials showed substantial evidence of the effectiveness of Xeglyze for the treatment of head lice infestation in patients 6 months of age and older. Although there are safe and effective treatment options currently available for the treatment of head lice infestation in patients 6 months of age and older, a need exists for treatment options with an acceptable safety profile that are effective after only a single treatment.

5 Risk Assessment

The primary safety population included 698 subjects from the Applicant's two completed Phase 3 trials, who were treated with either Xeglyze (n= 349) or Vehicle (n= 349). The primary safety

population included 495 pediatric subjects (age 6 months to < 18 years), of which, 239 were treated with Xeglyze and 256 were treated with Vehicle. The safety evaluation included adverse event reporting, evaluation by the investigator for local safety, full physical exams, and hematology and blood chemistry lab results.

The Applicant defined an adverse event (AE) as any untoward medical occurrence in a subject participating in a clinical trial. Specifically, an AE was any unfavorable and unintended sign, symptom, or disease temporally associated with the use of the study product, whether or not related to the study product.

5.1 SERIOUS ADVERSE EVENTS (SAES)

One SAE was reported during the pivotal trials for Xeglyze. The subject was treated with Vehicle in Phase 3 Trial Ha03-001. This subject had a medical history that included Type 1 diabetes, Stage 5 chronic kidney disease (CKD), anemia of CKD, diabetic gastroparesis with chronic vomiting, diabetic polyneuropathy and retinopathy, among other comorbidities. Investigators reported that the subject experienced renal impairment, and was hospitalized for permanent placement of a dialysis catheter and renal dialysis.

No subjects discontinued treatment due to an adverse event in any of the Phase 2 or Phase 3 studies.

5.2 ADVERSE EVENTS OF SPECIAL INTEREST (AESIS)

5.2.1 Potential Benzyl Alcohol Toxicity

The formulation of Xeglyze proposed for marketing contains the excipient benzyl alcohol (b) (4) (b) (4) benzyl alcohol per 200 g bottle of Xeglyze lotion) (b) (4) Systemic exposure to benzyl alcohol has been associated with headache, vertigo, nausea, vomiting, diarrhea, neonatal hyperbilirubinemia, metabolic acidosis, seizures, and respiratory distress. Neonates and low birth weight infants are at the greatest risk of increased absorption through their immature skin barrier and toxicity due to their inability to metabolize benzyl alcohol as quickly as older children and adults. Several cases of fatal toxic gasping syndrome due to systemic benzyl alcohol toxicity with other drug products have been reported in neonates who were administered intravascular normal saline that contained benzyl

alcohol as a preservative. [6] The minimum amount of benzyl alcohol at which toxicity may occur is not known. However, systemic exposure to benzyl alcohol at a concentration of approximately 109.2 µg/ mL (1.01 mmol/ L) has been associated with neonatal gasping syndrome.[7]

Due to the aforementioned risks, at the end of Phase 2, the Agency recommended the Applicant conduct a pediatric PK trial to evaluate the potential systemic exposure to benzyl alcohol. Serum benzyl alcohol concentrations were assessed in Trials Ha-03-003 and Ha-03-004. Benzyl alcohol was measurable in the serum of 7 out of 39 evaluable subjects, and the Cmax of benzyl alcohol in these 7 subjects ranged from 0.52 to 3.57 µg/mL. According to the Clinical Pharmacology reviewer, the maximum serum concentration of benzyl alcohol observed in the pediatric PK study is approximately 30-fold less than the serum concentration associated with neonatal gasping syndrome. Xeglyze use will not be recommended in patients under 6 months of age because of the potential for increased systemic absorption.

In order to mitigate the risk of accidental ingestion, Xeglyze will be marketed with a childproof container/closure system. Additionally, language recommending that Xeglyze only be administered to pediatric patients under the direct supervision of an adult will be included under the Warnings and Precautions (Section 5.1) and Patient Counseling Information (Section 17) of the Prescribing Information, and printed warnings will be included on both the carton and container.

5.2.2 Other Adverse Events of Special Interest

Potential Inhibition of CYP3A4

The primary metabolite of the active ingredient, abametapir carboxyl, is cleared slowly from the circulation. Because pediatric PK data were only collected up to 8 hours post-dose, and because

[6] Turner, M. A., Duncan, J. C., Shah, U., Metsvaht, T., Varendi, H., Nellis, G., ... & Mulla, H. (2014). Risk assessment of neonatal excipient exposure: Lessons from food safety and other areas. *Advanced drug delivery reviews*, *73*, 89-101.

[7] Clark K L. Division of Dermatology and Dental Products, Clinical Review of Xeglyze (abametapir), April 29, 2016.

concentrations of abametapir carboxyl were continuing to rise at that time, the Clinical Pharmacology reviewer concluded that Cmax and Tmax could not be characterized in pediatric subjects. However, the reviewer added, available data indicate that exposure to abametapir carboxyl is greater in pediatric subjects and is inversely proportional to weight. Studies using hepatocytes showed concentration-dependent inhibition of CYP3A4 and, to a lesser extent, CYP2B6 and CYP1A2 by abametapir carboxyl. The clinical review team is requesting a post-marketing requirement to address the potential inhibition of CYP3A4 by the carboxyl metabolite of the active ingredient.

Discoloration of Hair or Scalp

Three subjects in Phase 3 Trial Ha03-002 experienced red or pink hair discoloration after treatment with Xeglyze. The subjects were all from the same trial site in Mississippi. One subject had blonde hair and the other 2 had brown hair. These events all resolved within 7 days. The mechanism of action of Xeglyze involves chelation of metal cations, such as iron and zinc. In the presence of the ferrous (Fe^{+2}) ion, Xeglyze forms a water-soluble pink/red colored complex at iron concentrations as low as 1 ppm. Iron is commonly found in both well and tap water at varying concentrations. No subjects in the Vehicle group experienced this AE. The Applicant has included this AE in the proposed labeling.

6 Expected Postmarket Use

Xeglyze will be prescribed primarily in an outpatient setting. The Clinical Pharmacology review team will request a postmarketing requirement to address the potential inhibition of CYP3A4 by abametapir and its active metabolite, abametapir carboxyl.

7 Discussion of Need for a REMS

The safety of Xeglyze for the treatment of head lice was established from a database that included 698 patients. No major safety signals were identified for Xeglyze. Its safety profile appears to be similar to, or, have less of a risk for serious adverse events, than, what is reported for other approved treatments for head lice infestation. The most noteworthy safety concern is the potential toxicity related to the risk of increased systemic absorption of the excipient benzyl alcohol, which could, if absorbed to provide sufficient systemic levels of benzyl alcohol, lead to neonatal gasping syndrome in infants less than 6 months of age. However, the clinical data

suggests that toxic systemic levels are not likely to be observed when used in accordance with the label. Also, Xeglyze use will not be recommended in patients less than 6 months of age. Although the risk of benzyl alcohol toxicity when used topically according to the labelled directions appears low at this time, benzyl alcohol toxicity with this product could also result from accidental ingestion. In order to mitigate the risk of accidental ingestion, Xeglyze will be marketed with a child-resistant container-closure package, which is a well-established means of reducing accidental pediatric exposure. Additionally, language recommending that Xeglyze "should only be administered to pediatric patients under the direct supervision of an adult" will be included in the Warnings and Precautions and Patient Counseling Information sections of the Prescribing Information, and printed warnings will be included on both the carton and container. The measures were reviewed by the Division of Medication Error Prevention and Analysis (DMEPA), and the reviewer recommended changes to the Applicant's proposed labels and labeling, in order to adequately reduce the risks of accidental pediatric ingestion.[8] The Applicant incorporated DMEPA's recommended changes. DRISK and DDDP concurred that a REMS is not necessary to ensure the benefits of Xeglyze outweigh the risks.

8 Conclusion & Recommendations

At this time, risk mitigation measures beyond professional labeling are not warranted for Xeglyze for the treatment of head lice infestation in patients 6 months of age and older. According to the Clinical reviewer, Xeglyze demonstrated substantial evidence of efficacy for the proposed indication. Based on the risks associated with Xeglyze in the clinical trials, a REMS is not necessary to ensure the benefits outweigh the risks for Xeglyze. If new safety information becomes available, please consult DRISK.

9 Appendices

9.1 References

[8] Mehta H. Division of Medication Error Prevention and Analysis, Label, Labeling and Packaging Review for Xeglyze (abametapir), March 16, 2016.

- Hatchtech. Original submission NDA 206966, received September 14, 2015.
    - Section 2.5, Clinical Overview
    - Section 2.7.3, Summary of Clinical Efficacy
    - Section 2.7.4, Summary of Clinical Safety
- Hatchtech. Proposed Prescribing Information for Xeglyze (abametapir), received September 14, 2015; updated on December 16, 2015, February 19, 2016, and May 13, 2016.
- Dr. Reddy's Laboratories, SA. 120-Day Safety Update Report for Xeglyze (abametapir), received January 20, 2016.
- Mehta H. Division of Medication Error Prevention and Analysis, Label, Labeling and Packaging Review for Xeglyze (abametapir), March 16, 2016.
- Tran D C. Division of Clinical Pharmacology 3, Clinical Pharmacology Review of Abametapir lotion, 0.74% w/w, dated April 26, 2016.
- Clark K L. Division of Dermatology and Dental Products, Clinical Review of Xeglyze (abametapir), April 29, 2016.
- Late Cycle Meeting Background Package for Xeglyze, May 20, 2016.

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