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Eric Bastings, MD, Deputy Director
U.S. Food and Drug Administration
Office of Drug Evaluation I, Division of Neurology Products
Center for Drug Evaluation and Research (CDER)
Central Document Control Room
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

Product Name:	**Cambia® (diclofenac potassium) 50 mg powder for oral solution**
NDA No.:	**022165**
Sequence No.:	**0065**
Subject:	**RESPONSE TO PREA NON-COMPLIANCE LETTER PREA DEFERRAL EXTENSION REQUEST**

Dear Dr. Dunn:

Depomed, Inc. (Depomed) has received the Division's January 9, 2017 Notification of Non-Compliance with PREA regarding PMRs 974-4, 974-5, and 974-6 under NDA 022165 for Cambia (diclofenac) powder for oral solution, which was originally approved on June 17, 2009. The 3 pediatric assessment PMRs in question were originally assigned to Kowa Pharmaceuticals America, Inc. (Kowa), the original sponsor of NDA 022165, as deferred pediatric studies with final due dates of December 31, 2016.

Depomed wishes to remind the Division that the original approval of NDA 022165 on June 17, 2009 was accompanied by the assignment of 6 deferred pediatric PMRs assigned to the sponsor, Kowa. The first 3 deferred pediatric PMRs 974-1, 974-2, and 974-3 were assigned deferred completion dates of June 2013 (4 years after the original approval of NDA 022165). These 3 PMRs focused on the assessment of Cambia in pediatric patients with migraine with or without aura ages 12 years to 17 years. The second 3 deferred PMRs 974-4, 974-5, and 974-6, assigned deferred completion dates of June 2016 (7 years after the original approval of NDA 022165), focused on the assessment of Cambia in pediatric patients with migraine with or without aura ages 6 years to 11 years. It is noted that the 3 PMRs focused on pediatric patients aged 6 years to 11 years, the same 3 PMRs which are the subject of the Division's January 9, 2017 Notice of Non-Compliance with PREA, were identified as studies where it was stated in the NDA approval letter that "Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, *we* will make a determination as to whether or not pediatric studies are practicable for this age range". This description of PMRs 974-4, 974-5 and 974-6 defines that these 3 studies should only be initiated after the completion of the studies identified as PMRs 974-1, 974-2 and 974-3. The conduct of PMRs 974-1, 974-2, and 974-3 was not initiated by the original

sponsor, Kowa, or by the subsequent sponsor, Nautilus Neurosciences (Nautilus). In fact, Nautilus requested 2 deferral extensions for the 6 pediatric PMRs on March 29, 2013 and August 14, 2013, both of which were denied by the Division. Nautilus further received a Notification of Non-Compliance with PREA on July 3, 2013 based on the failure of Nautilus to complete PMRs 974-1, 974-2, and 974-3 by the deferred completion date of June 2013. Depomed accepted the sponsorship of NDA 22-165 on December 17, 2013.

Depomed takes the pediatric PMRs for Cambia under NDA 022165 very seriously and has progressed diligently with the planning and conduct of these studies since assuming NDA sponsorship. On April 9, 2014, Depomed held a Type B Meeting with the Division to discuss the design and conduct of protocol 81-0076, designed to meet the requirements of PMR 974-1. This study was subsequently initiated and has now been completed (Depomed will be submitting the study report for this study in the coming weeks). Depomed initiated discussions with the Division on the design of study 81-0077, designed to meet the requirements of PMR 974-2, through a Type C Meeting (written response only) leading to the Division's written response of October 29, 2014. The final design and conduct of study 81-0077 requires the outcomes of the 81-0076 study in order to determine the most appropriate doses to study in the efficacy study. Now that the 81-0076 study has been completed, Depomed will be submitting a final proposed protocol for study 81-0077 within the coming weeks.

As described, Depomed is progressing through the initial 3 PMRs studying Cambia in pediatric patients ages 12 years to 17 years. As identified in the original approval letter for NDA 022165, Depomed intends to discuss the practicality of PMRs 974-4, 974-5 and 974-6 with the Division following the completion of the studies planned to meet the requirements of the initial 3 PMRs 974-1, 974-2, and 974-3. Again, we remind the Division that Depomed became the sponsor of NDA 022165 in December 2013 (4.5 years after the initial approval of NDA 022165 and the assignment of the subject PMRs), at which time there had been no progress on the design and conduct of any of the assigned pediatric PMRs by the previous sponsors. Since that time, Depomed has demonstrated, through the planning and conduct of the initial studies in pediatric patients ages 12 years to 17 years, our ongoing commitment to, and continued progress with, the assigned pediatric PMRs under NDA 022165.

With this response to the Division's Notice of Non-Compliance with PREA, Depomed would like to formally request a deferral extension for the 6 assigned pediatric PMRs under NDA 022165 to allow Depomed sufficient time to address and complete these studies in a time frame consistent with that originally planned at the time of NDA approval. Accounting for Depomed's lost time in PREA study preparation before we became the sponsor of NDA 022165, Depomed now proposes the following extended deferred dates for the completion of the 6 assigned PMRs:

974-1 Deferred safety and pharmacokinetic pediatric study under PREA in pediatric patients with migraine with or without aura ages 12 years to 17 years.

Final Report Submission: June 2017

974-2 Deferred controlled effectiveness study under PREA for the acute treatment of migraine attacks with or without aura in pediatric patients ages 12 years to 17 years.

Final protocol submission: June 2017

Clinical Trial Start Date: December 2017

Final Report Submission: December 2019

974-3 Deferred long-term open label safety study in pediatric patients with migraine with or without aura ages 12 years to 17 years.

Final protocol submission: June 2017

Clinical Trial Start Date: December 2017

Final Report Submission: December 2019

974-4 Deferred safety and pharmacokinetic pediatric study under PREA in pediatric patients with migraine with or without aura ages 6 years to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

Final protocol submission: December 2019

Clinical Trial Start Date: June 2020

Final Report Submission: June 2023

974-5 Deferred controlled effectiveness study under PREA for the acute treatment of migraine attacks with or without aura in pediatric patients ages 6 years to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

Final protocol submission: December 2020

Clinical Trial Start Date: June 2021

Final Report Submission: June 2023

974-6 Deferred long-term open label safety study under PREA in pediatric patients with migraine with or without aura ages 6 years to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

Final protocol submission: December 2020

Clinical Trial Start Date: June 2021

Final Report Submission: June 2023

Again, Depomed is committed to working with the Division towards the timely conduct and completion of the assigned pediatric PMRs under NDA 022165. We appreciate the Agency's consideration of this request for deferral extension based upon the described circumstances and Depomed's demonstrated activities to progress these assigned pediatric study requirements.

If you have any questions regarding this response, please do not hesitate to contact me at (510) 744-8639, or RA@depomed.com.

Sincerely,

Greg Bates, DVM
Vice President, Regulatory Affairs
Depomed, Inc.

Electronic Submission Specifications

This submission is compliant with FDA's Guidelines for Industry and current eCTD specifications.

All files were checked and verified to be free of viruses prior to transmission through the electronic submission gateway.

Anti-Virus Program	Symantec Endpoint Protection Edition
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