August 5, 2021

Nick Kozauer, MD, Director
Division of Neurology II
Office of Neuroscience
Center for Drug Evaluation and Research
10903 New Hampshire Avenue,
Building 22, Suite 4346
Silver Spring, MD 20993

RESPONSE TO PREA NONCOMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

Re: TREXIMET (sumatriptan and naproxen sodium) Tablets
NDA 021926/SN0182

Dear Dr. Kozauer:

Reference is made to Currax Pharmaceuticals LLC's New Drug Application (NDA) 021926 for TREXIMET (sumatriptan and naproxen sodium) Tablets indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older. Reference is also made to the Noncompliance letter received on June 24, 2021, regarding the deferred pediatric assessment PMR 2910-2 assigned to NDA 021926 under the Pediatric Research Equity Act (PREA). This submission includes our formal response to the Non-Compliance Letter mentioned above and a Request for Deferral Extension.

TREXIMET was approved on April 15, 2008 for the acute treatment of migraine attacks with or without aura in adults. The approval letter states:

"The findings in adults, and on which the current approval is based, demonstrate sufficient safety to proceed with pediatric studies in children ages 12 years to 17 years. Pediatric studies in children ages 6 years to up to 11 years should be delayed until additional safety and effectiveness data have been collected in older children and we make a determination whether pediatric studies are practicable for children ages 6 years to 11 years."

On November 14, 2014, Pernix Ireland Limited (Pernix), the previous NDA holder, submitted a Prior Approval supplement dated (S-012) to fulfill pending postmarketing requirements and also to include a lower strength for children in the 12 to 17 years of age group. The supplement was approved May 15, 2015 and the following new postmarketing requirements were assigned by the Agency:

2910-1 Conduct a juvenile rat toxicology study to identify the unexpected serious risk of adverse effects of sumatriptan/naproxen on postnatal growth and development. The study should utilize animals of an age range and stage(s) of development that are comparable to the intended pediatric population; the duration of dosing should cover the intended length of treatment in the pediatric population. In addition to the usual toxicological parameters, this study must evaluate effects of sumatriptan/naproxen on growth, reproductive development, and neurological and neurobehavioral development.

Final Protocol Submission: November 2016
Study Completion: November 2017
Final Report Submission: May 2018

2910-2 Conduct a pharmacokinetics (PK) study in children ages ≥6 years to 11 years with migraine. Using information from this PK study, conduct a controlled efficacy study in children ages ≥6 years to 11 years with migraine. Conduct a long-term open-label safety study in pediatric patients with migraine ages ≥6 years to 11 years. The long-term safety study must provide a descriptive analysis of safety data in at least 50 pediatric patients treated with Treximet for a duration of at least 6 months, treating on average at least one migraine attack per month, at doses evaluated in the efficacy study.

Final Protocol Submission: November 2016
Study Completion: November 2020
Final Report Submission: May 2021

Pernix submitted the Request for Pediatric Study Waiver (for ages 6-11), dated January 12, 2016. This request was based on the company's concerns that the additional required pediatric studies were impracticable, and that TREXIMET was unlikely to be used in a substantial number of pediatric patients ages 6-11. FDA's PREA Waiver Denied notice, dated December 12, 2016, denying Pernix's request for a waiver of pediatric postmarketing study requirements for ages 6-11.

The second Request for Pediatric Study Waiver (for ages 6-11) was submitted on July 6, 2017 requesting that the Agency reconsider Pernix's prior waiver request. The PREA Waiver Denied letter was received on October 24, 2018.

On April 30, 2019, Currax Pharmaceuticals LLC (Currax) acquired certain assets of Pernix Therapeutics, including IND 068436 and NDA 021926.

Several challenges have caused a delay in fulfilling these PMRs. (1) The study has already been delayed before the acquisition. Noted, the final report of a juvenile rat toxicology study was due on May 2018. However, the PREA Waiver Denied letter was not received until October 2018. (2) After the acquisition, Currax immediately evaluated the status and initiated the plan to fulfill

the requirements. However, COVID-19 pandemic further delayed our process in selecting the laboratory to conduct the toxicology studies.

Currax recognizes the importance of the PREA program. As of today, our team has completed the laboratory selection process for conducting the juvenile rat toxicology study. We plan to start the study immediately once the protocol is reviewed and approved by the Agency.

Currax remains committed to fulfilling the postmarketing requirements under PREA. We hereby request a Deferral Extension for PMR 2910-1 and PMR 2910-2 with the proposed dates set forth below.

PMR 2910-1: Conduct a juvenile rat toxicology study

Final Protocol Submission: November 2021

Study Completion: February 2023

Final Report Submission: May 2023

PMR 2910-2: Conduct a pharmacokinetics (PK) study, an efficacy study, and a long-term safety study in children ages ≥6 years to 11 years with migraine.

Final Protocol Submission: June 2023

Study Completion: June 2026

Final Report Submission: December 2026

As requested by the FDA a cross-reference letter to this submission will also be submitted to IND 068436.

If you have any questions about this submission, please feel free to contact me at (862) 579-2848 or via email at jfan@curraxpharma.com.

Sincerely,

Joyce Fan
Digitally signed by Joyce Fan
Date: 2021.08.05 17:38:53 -04'00'

Joyce Fan
Director, Regulatory Affairs
Currax Pharmaceuticals LLC
155 Franklin Road, Suite 450,
Brentwood, TN 37027
Phone: 862-579-2848
Email: jfan@curraxpharma.com

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Anti-Virus Program	Windows Security
Security Intelligence Version	1.343.2244.0
Virus Definition Date	8/4/2021
Submission Size	Approx. 2 MB