15 January, 2020

Sumathi Nambiar, M.D., MPH, Director
Division of Anti-infective Products
Center for Drug Evaluation and Research,
Food and Drug Administration
5901-B Ammendale Rd.
Beltsville, MD 20705-1266
ATTN: J. Christopher Davi, Senior Regulatory Project Manager

RE: **NDA 022110 VIBATIV® (telavancin) Injection (SN0197)**
RESPONSE TO PREA NONCOMPLIANCE LETTER (PMR 1995-1)
(IND 060237)

Dear Dr. Nambiar,

Reference is made to NDA 022110 for VIBATIV® (telavancin) Injection. VIBATIV is approved for the treatment of adult patients with complicated skin and skin structure infections (cSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-susceptible and -resistant isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus group (includes S. anginosus, S. intermedius, and S. constellatus), or Enterococcus faecalis (vancomycin-susceptible isolates only) and, hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP), caused by susceptible isolates of Staphylococcus aureus (including methicillin-susceptible and -resistant isolates). VIBATIV should be reserved for use when alternative treatments are not suitable.

Reference is also made to the Notification on Non-Compliance with PREA correspondence (Reference ID: 4530313) dated 12 December, 2019. Cumberland's response to this correspondence is as follows.

On 18 September, 2019, Cumberland sent an e-mail to Christopher Davi, Senior Regulatory Project Manager addressing this matter (see below). A copy of this e-mail is located in Section 1.17.2.

"Per previous discussions with the Agency and recent changes to the PREA PMRs for NDA 022110, Cumberland intends to submit the following to IND 060237 by 30 September 2019:

- [redacted] (b) (4)

- An amended study protocol for PMR 1995-001 (study 0101), [redacted] (b) (4)

In addition, the following will submitted to NDA 022110:

(b) (4)

We had originally planned to address a deferral request for PMR 1995-001 (b) (4)

This was discussed with the Agency on 29 May, 2019 in a teleconference. We were originally advised to submit in the near future a separate/new Request for Deferral Extension for PMR 1995-001. This submission was to include the following:

(b) (4)

However, we received a deferral extension denial by the Agency on 17 July, 2019 in response to a deferral request submitted in April 2019 (SN0186) to extend the timeline because of our recent acquisition of the Application in November of 2018. Since the acquisition, we amended study protocol 0101 in order to increase enrollment potential (Amend. 04, SN0374, IND 060237, submitted 05 March 2019).

As history of the previous Sponsor's attempts to fulfill the PMRs, Theravance Biopharma (Theravance), launched VIBATIV in the United States on 05 November 2009. Shortly thereafter, VIBATIV distribution was placed on voluntary hold from November 2011 to August 2013 (b) (4) VIBATIV was reintroduced to the U.S. market in August 2013 following approval of a new contract drug product manufacturer (Reference ID: 3316822, 31 May 2013). Due to the lack of availability of study drug as well as slow recruitment in the single-dose pediatric PK study, the Agency granted an extension of pediatric study timelines for PMRs 1995-001, 1995-002 and 1529-001 (Reference ID: 3660456, 19 November 2014). On 31 January 2017, the Agency granted an additional deferral for PMR 1995-001 (Reference ID: 4049502) due to delays involving study participants, sites, and/or management. Most recently, a deferral was granted on 06 December 2017 (Reference ID: 4190480) for both PMRs 1995-001 and 1995-002 because of continued enrollment challenges. The December 2017 deferral also modified the required age cohorts so that PMR 1995-001 includes patients ≥3 months old and PMR 1995-002 includes patients aged 0 to < 3 months. The study was to be completed in June 2019 with the clinical study report submitted in September 2019.

In previous conversations with the Agency, it has been acknowledged that PMR 1995-001 is ongoing and would likely continue past the September 2019 PMR deadline. We acknowledge the Agency's desire to see progress on PMR 1995-001 given the three deferral extension letters that were granted to the previous sponsor and have acted to hopefully expedite this inherited study.

(b) (4)

(b) (4)

The Deferral Extension Denied letter references that a noncompliance letter pursuant to 505B9(D)(1) could be issued by the Final Report Submission date, which is September 2019. Given the July denial letter as well as the ongoing study status of PMR 1995-001, Cumberland seeks advice on what specific steps need to be taken in order to maintain compliance with PMR requirements. Additionally, as the data lock point was earlier this month, how should the study status for PMR 1995-001 be listed in the upcoming annual report for NDA 022110?

(b) (4)

Despite multiple efforts to progress this study, Cumberland has not been able to complete enrollment. And, since a deferral extension request was denied by the Agency on 17 July, 2019 in response to a deferral request submitted in April 2019, we would appreciate any advice the Agency can provide to move forward.

Per the PREA Noncompliance correspondence, we are submitting this information to our NDA with a cross-reference letter to the Investigational New Drug Application (IND) to which the protocol was submitted.

All electronic files included in this submission are less than 6 MB. All files were checked and verified to be free of viruses, prior to being transmitted using Symantec Antivirus Corporate Edition, program version 14.2.4814.1101 with a virus definition date of January 7, 2020 revision 2.

Cumberland considers the data submitted with this application to be trade secret and protected from disclosure under the provisions of 21 CFR 312.130 and 314.430.

A signed FDA Form 356h is attached. If you have any questions, please feel free to contact me by phone (615) 255-0068, by email at bzaborny@cumberlandpharma.com or fax (866) 438-2372.

Sincerely,

Digitally signed by Beth A. Zaborny
DN: cn=Beth A. Zaborny, o=Cumberland Pharmaceuticals Inc., ou=Regulatory Affairs, email=bzaborny@cumberlandpharma.com, c=US
Date: 2020.01.09 15:40:26 -06'00'

Beth A. Zaborny
Director, Regulatory Affairs

CUMBERLAND PHARMACEUTICALS INC.
2525 West End Avenue, Suite 950 • Nashville, Tennessee 37203 • Telephone: (615) 255 0068 • Facsimile: (615) 255 0094
www.cumberlandpharma.com