

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

208744Orig1s000

OTHER ACTION LETTERS



NDA 208744

COMPLETE RESPONSE

Accord Healthcare Inc.
Attention: Sabita Nair
Sr. Director-Regulatory Affairs
1009 Slater Rd, Suite 210-B
Durham, NC 27703

Dear Ms. Nair:

Please refer to your New Drug Application (NDA) dated September 30, 2015, received September 30, 2015, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Tigecycline for Injection, USP 50 mg/vial.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY

1. Your application references Drug Master File (DMF) (b) (4). This DMF was found inadequate to support your submission and a deficiency letter was sent to the DMF holder on December 7, 2015. These deficiencies must be adequately addressed before this application can be approved. In your response to this letter, include the date the DMF holder amended the DMF to address the deficiencies.
2. The proposed expiration dating of 24 months for the drug product, Tigecycline for Injection, is not supported by the currently available stability information. Provide updated stability data for the three drug product registration batches to support the proposed drug product expiration dating.
3. Provide results of the extractable and leachable studies for the proposed (b) (4) using suitable solvents and the reconstituted solutions of the proposed drug product, Tigecycline for Injection, with the proposed reconstitution agents.

FACILITY INSPECTIONS

4. During a recent inspection of the (b) (4) manufacturing facility for this NDA, our field investigator observed objectionable conditions at the facility and conveyed that information to the representative

of the facility at the close of the inspection. Satisfactory resolution of these deficiencies is required before this NDA may be approved.

PATENT

5. The listed drug upon which your application relies is subject to a period of patent protection and therefore final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be made effective until the period has expired.

Your application contains certifications to each of the patents under section 505(b)(2)(A)(iv) of the Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of, this drug product under this application (“Paragraph IV certifications”).

Section 505(c)(3)(C) of the Act provides that approval of a new drug application submitted pursuant to section 505(b)(2) of the Act shall be made effective immediately, unless an action is brought for infringement of one or more of the patents that were the subject of the paragraph IV certifications. This action must be taken prior to the expiration of forty-five days from the date the notice provided under section 505(b)(3) is received by the patent owner/approved application holder. You notified us that you complied with the requirements of section 505(b)(3) of the Act.

In addition, you have notified the Agency that the patent owner and/ or approved application holder has initiated a patent infringement suit against you with respect to patents 7879828, 8372995 and 8975242 in the United States District Court for the District of Delaware (Pfizer Inc., Wyeth LLC, Pfizer Pharmaceuticals LLC, PF Prism C.V. and Pfizer Manufacturing Holdings LLC Plaintiffs, v. Accord Healthcare, Inc., Accord Healthcare Ltd., and Intas Pharmaceuticals Ltd., Defendants). Therefore, final approval cannot be granted until:

1. a) expiration of the 30-month period provided for in Section 505(c)(3)(C) beginning on the date of receipt of the 45-day notice required under Section 505(b)(3), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or
 - b) the date the court decides that the patents are invalid or not infringed as described in section 505(c)(3)(C)(i), (ii), (iii,) or (iv) of the Act, or,
 - c) the listed patents have expired, and
2. we are assured there is no new information that would affect whether final approval should be granted.

PRESCRIBING INFORMATION

6. We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Physician Labeling Rule

requirements for prescribing information and Pregnancy and Lactation Labeling Final Rule websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the prescribing information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

ADDITIONAL COMMENTS

Your application includes a Comparability Protocol that provides (b) (4). Since the information currently provided for the drug substance is inadequate due to deficiencies in DMF (b) (4), the proposed Comparability Protocol cannot be evaluated at this time and should be included for review in your complete response.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies/clinical trials for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.
 - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
6. Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
7. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
8. Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry, "Formal Meetings Between FDA and Sponsors or Applicants," May 2009 at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf>.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Deepak Aggarwal MS, MSPH, Regulatory Project Manager, at (301) 796-0746.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SUMATHI NAMBIAR
07/22/2016