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RESEARCH**

APPLICATION NUMBER:
050824Orig1s000

OTHER ACTION LETTERS



NDA 50-824

COMPLETE RESPONSE

DAVA Pharmaceuticals, Inc.
Attention: Susan Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, NJ 07024

Dear Ms. Hamet:

Please refer to your New Drug Application (NDA) dated September 21, 2009, received September 22, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for the co-packaging of omeprazole delayed-release capsules, 20 mg, clarithromycin tablets, 500 mg and amoxicillin capsules, 500 mg.

We acknowledge receipt of your amendments dated:

October 12, 2009	November 20, 2009	November 27, 2009
November 30, 2009	December 1, 2009	January 6, 2010
January 18, 2010	January 19, 2010	March 19, 2010
March 23, 2010	April 20, 2010	May 6, 2010
June 9, 2010	June 18, 2010	

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.

PEDIATRIC PLAN

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

The proposed pediatric plan included in your original submission contained a request and justification (b)(4) waiver of pediatric studies for your co-packaging of omeprazole/clarithromycin/amoxicillin product. Your justification (b)(4) was found inadequate and on October 26, 2009, we issued correspondence requesting that you submit a revised pediatric plan, and included a description of the type of justification needed (b)(4)

(b) (4) This correspondence also requested that you respond by November 30, 2009.

You provided a revised pediatric plan on January 18, 2010 (b) (4). We did not agree with your justification; therefore on May 11, 2010, we issued a correspondence requesting the submission of a revised pediatric plan. In this request, we noted there is currently no approved therapy for the treatment of pediatric patients with *H. pylori* infection and duodenal ulcer disease; therefore, we asked that you submit a revised pediatric plan that outlines the proposed pediatric studies and the development of an age-appropriate formulation, with inclusion of the timeline for completion of such studies. We asked that this information be submitted by June 7, 2010. As of the date of this letter, we have not received your revised pediatric plan.

To address this deficiency, please, submit your pediatric drug development plan along with a request for deferral of pediatric studies as requested in our correspondence of May 11, 2010. The pediatric development plan is for the indication of treatment of *H. pylori* infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) to eradicate *H. pylori*. Eradication of *H. pylori* has been shown to reduce the risk of duodenal ulcer recurrence,

LABELING

We have reviewed the labeling of your product, including package insert, and carton and container labeling. Before we can approve your application, you will need to submit the following labeling information:

1. Submit draft labeling (package insert) that incorporates revisions described in the attached labeling (package insert). In addition, submit 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>. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should include annotations that support any proposed changes.
2. Submit draft color copies of carton and container labeling revised as described in our correspondence dated July 6, 2010. A copy of this correspondence is attached to this letter.
3. Submit labeling (package insert) for the amoxicillin capsules, ANDA 62-881, that you intend to use in your co-packaged product, so that we may compare the description of the amoxicillin in the ANDA with the description in your co-package product.

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.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference 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's "Guidance for Industry - Formal Meetings Between the 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 Judit Milstein, Chief Project Management Staff, at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURES: Proposed Content of Labeling (Package Insert)
 Copy of correspondence dated July 6, 2010

36 pages of draft labeling has been withheld in full as B(4) CCI/
TS immediately following this page

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	OMEPRAZOLE 25MG/AMOXOCILLIN 500MG/CLARITHROMYCIN 500MG

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

/s/

RENATA ALBRECHT
07/20/2010