DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 22-106

NDA APPROVAL

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Catherine Glamkowski
Associate Director, North American Regulatory Liaison
920 U.S. Highway 202
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Glamkowski:

Please refer to your new drug application (NDA) dated December 12, 2006, received December 13, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for DORIBAX™ (doripenem for injection).

We acknowledge receipt of your submissions dated January 30, March 30, April 9, 11, 12 (2), May 17, 18, 30, June 4, 6, 22, July 3, 12, 27, August 9, 10 (2), 17, 24, 28, September 4 (3), 13, 18, and October 2 and 8.

This new drug application provides for the use of DORIBAX™ (doripenem for injection) for the treatment of complicated intra-abdominal (cIAI)) and complicated urinary tract (cUTI) infections caused by susceptible isolates of the designated microorganisms.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at *http://www.fda.gov/oc/datacouncil/spl.html* that is identical to the enclosed labeling (text for the package insert) dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 22-106."

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22-106**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 0 to18 years until October 12, 2012.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

1. Deferred pediatric studies under PREA for the treatment of cUTI in pediatric patients ages 0-18 years.

   Final Report Submission: October 12, 2012

2. Deferred pediatric studies under PREA for the treatment of cIAI in pediatric patients ages 0-18 years.

   Final Report Submission: October 12, 2012

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitments must be clearly designated "**Required Pediatric Study Commitments**".

We remind you of your postmarketing study commitments in your submission dated October 11, 2007. These commitments are listed below.

3. Conduct post-marketing surveillance study (such as a patient registry) regarding hemolytic anemia, renal failure/renal impairment, and seizures in doripenem-treated subjects.

Protocol Submission:	by June, 2008
Study Start:	by March, 2008
Final Report Submission:	by December, 2012

4. Conduct a Phase 1 study to assess potential interactions between doripenem and valproic acid.

Protocol Submission:	by December, 2007
Study Start:	by March, 2008
Final Report Submission:	by December, 2008

5. Conduct US surveillance studies for two years from the date of marketing DORIBAX to determine if resistance to doripenem has developed in those organisms specific to the indications in the label for complicated urinary tract infection and complicated intra-abdominal infection. The US surveillance studies on *Klebsiella pneumoniae* isolates should include monitoring for the presence of the KPC carbapenemase.

Protocol Submission:	by December, 2007
Study Start:	Ongoing
Final Report Submission:	by March, 2010

6. Conduct studies to define the mechanism(s) of resistance for isolates identified as being resistant to doripenem during the surveillance period (two years from the date of marketing).

Protocol Submission:	Not applicable
Study Start:	by March, 2008
Final Report Submission:	by March, 2010

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

NDA 22-106 was not referred to an advisory committee for review for the following reasons: There are three previously approved antimicrobial agents in the carbapenem class. Evaluation of the safety data did not reveal particular safety issues that were unexpected for the carbapenem class, and the design and results of the efficacy trials did not pose particular concerns. Doripenem is an intravenous agent studied for more serious infections for which there is adequate justification for using an active controlled study designed to show non-inferiority.

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of

promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

In addition, we request that you submit one copy of the introductory promotional materials you propose to use for this product to this division.

Please submit one market package of the drug product when it is available.

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Susmita Samanta, MD, Regulatory Project Manager, at (301) 796-1400.

Sincerely,

{See appended electronic signature page}

Edward Cox, MD, MPH
Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure

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

/s/

Edward Cox

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