CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
21-337

Trade Name: Invanz I.V. or I.M.

Generic Name: ertapenem sodium

Sponsor: Merck & Co., Inc.

Approval Date: November 21 2001

Indications: Provides for the use of Invanz I.V. and I.M. for the following indications:

1. Complicated Intra-abdominal infections.
2. Complicated Skin and Skin Structure Infections.
3. Community Acquired Pneumonia
4. Complicated Urinary Tract Infections including pyelonephritis.
5. Acute Pelvic Infections including postpartum endomyometiritis, septic abortion and post surgical gynecologic infections.

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APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-337

Merck & Co., Inc.
Attention: Michelle Kloss, Ph.D.
Senior Director, Regulatory Affairs
P.O. Box 4
Sumneytown Pike, BLA-20
West Point, PA 19486

Dear Dr. Kloss:

Please refer to your new drug application (NDA) dated November 30, 2000, received November 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for INVANZ™ (ertapenem sodium) for intravenous or intramuscular use.

We acknowledge receipt of your submissions dated December 14, and 19, 2000; January 10, 16, 18, 24, and 29; February 9, 13, 22, 27, and 28; March 7 (2), 13, 15, 22, and 30; April 4, and 9; May 4, 7 (2), 16, 21, 24, 25, 29 (2), and 31; June 5, 6, 8 (2), 12, 14, 19, 20, and 22 (2); July 3, 6, 13 (2), 16, 17, 18 (2), 19, 26, 30 and 31; August 1, 14, 22, 24, and 30; September 4, 14, 17, 18, 21 (2), 26, 27, and 28; October 1, and 3; November 7, 15 (2), and 19, 2001.

This new drug application provides for the use of INVANZ™ (ertapenem sodium) I.V. and I.M. for the following indications:

1. Complicated Intra-abdominal Infections
2. Complicated Skin and Skin Structure Infections
3. Community Acquired Pneumonia
4. Complicated Urinary Tract Infections including pyelonephritis
5. Acute Pelvic Infections including postpartum endomyometritis, septic abortion and post surgical gynecologic infections.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and submitted draft labeling (immediate container and carton labels submitted November 30, 2000). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21337." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated November 19, 2001. These commitments are listed below.

1. **Commitment #1**:

   Submit the final study report for Protocol 035 "A Randomized, Double-Blind, Parallel-Panel, Placebo-Controlled Study to Investigate the Effects of Maximum Plasma Concentrations of MK-0826 on QTc Interval Following Single IV Dose Administration in Healthy Subjects."

   Final Report Submission: By May 30, 2002

2. **Commitment #2:**

   Conduct a prospective, multicenter, double-blind, randomized, comparative study (with piperacillin/tazobactam 3.375 gm every 6 hours as the comparator) that assesses mortality at the end of parenteral therapy, 14 days post study therapy, and at 4-6 weeks post therapy in adult patients with complicated intra-abdominal infections. Inclusion and exclusion criteria should be similar to those used in Protocol 017 to ensure that patients with similar types of infections and severity of infection will be enrolled. The final study report for this study should be submitted prior to May 31, 2004.

Final Protocol Submission:	Within 3 months of the date of this letter
Study Start:	Within 6 months of the date of this letter
Final Report Submission:	By May 31, 2004

Submit clinical protocols to your IND for this product. Submit 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 must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

Please note, based on the data submitted and reviewed, the product has an expiration date of 18 months.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We acknowledge receipt on February 10, 2000 of your revised Proposed Pediatric Study Request (PPSR). We are deferring submission of your pediatric studies until November 30, 2004.

We wish to remind you that the Agency issued a written request for ertapenem on May 15, 2000, for pediatric studies to be conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act. Please note that the FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as is required to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Anti-Infective Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Maureen Dillon-Parker, Project Manager, at (301) 827-2125.

Sincerely,

{See appended electronic signature page}

Mark Goldberger, M.D.
Acting Director
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure - Labeling

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

/s/

Mark Goldberger
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