DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21-821/S-026 and S-031

SUPPLEMENT APPROVAL

PF PRISM C.V.
c/o Pfizer Inc.
Attention: Nadia Kirzecky
Director, Worldwide Safety and Regulatory
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Kirzecky:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA#/Drug Name	Supplement Number	Submission Date	Date Received
NDA 21-821/Tygacil (tigecycline) for Injection	S-026 S-031	September 30, 2009 February 11, 2011	September 30, 2009 February 11, 2011

We acknowledge receipt of your amendments to these supplemental applications dated November 29, 2011, February 7, 2012 [S-031 only], and February 13, July 3, and September 23, 2013.

Supplemental application S-026 is a "Prior Approval" supplement that provides for changes to the **INDICATIONS AND USAGE** section stating that Tygacil is not indicated for the treatment of diabetic foot infections.

Supplemental application S-031 is a "Changes Being Effected" supplement that provides for changes to the **ADVERSE REACTIONS** section of the labeling to include the adverse reactions of pneumonia and severe skin reactions, including Stevens-Johnson syndrome.

In addition to the changes requested in the above supplements, the attached labeling also includes the following changes as discussed with you via multiple electronic communications (e-mails) and finalized in your submission containing revised draft labeling on September 23, 2013.

- Addition of a "**BOXED WARNING**" to include information from meta-analysis of clinical trials that showed an increased risk of mortality in Tygacil-treated patients and to reserve Tygacil for use in situations when alternative treatments are not suitable.
- Addition of **Limitations of Use** (1.4) to include information that Tygacil is not indicated for the treatment of diabetic foot infections and hospital-acquired or ventilator-associated pneumonia.
- Revisions of the **DOSAGE AND ADMINISTRATION** section (2), **Pediatric Patients** subsection (2.3) and **USE IN SPECIFIC POPULATIONS** section (8.0), **Pediatric Use** subsection (8.4) to include information about use in the pediatric population.
- Revisions to the **WARNINGS AND PRECAUTIONS** section (5), **All-Cause Mortality** subsection (5.1) regarding the increased risk of mortality.
- The following revisions to the **ADVERSE REACTIONS** section (6):
    - **Clinical Trials Experience** subsection (6.1) to include information about an increase in mortality in trials conducted for approved indications
    - **Post-Marketing Experience** subsection (6.2), to include adverse reactions of Stevens-Johnson syndrome and symptomatic hypoglycemia
    - Revised the incidence of adverse reactions in Table 1.
- Addition of a **Pharmacodynamics** subsection (12.2), **Cardiac Electrophysiology**, to the **CLINICAL PHARMACOLOGY** section (12).
- Minor editorial changes including updates to the **REFERENCES** (15) section.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for package insert, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in these supplemental applications, as well as annual reportable changes and annotate each change. 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 provide appropriate annotations, including supplement number(s) and annual report date(s).

PROMOTIONAL MATERIALS

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

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

If you have any questions, call Carmen DeBellas, PharmD, R.Ph., Regulatory Project Manager, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE:
Content of Labeling

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
09/26/2013