

NDA 021266/S-047
NDA 021267/S-057
NDA 021630/S-036

SUPPLEMENT APPROVAL

PF PRISM C.V.
c/o Pfizer Inc.
Attention: Anna Maria Gambino, MBA
Director, Global Regulatory Affairs
Hospital Business Unit
Pfizer Biopharmaceutical Group
235 East 42nd Street
New York, NY 10017

Dear Ms. Gambino:

Please refer to your supplemental new drug applications (sNDAs) dated March 2, 2020, received March 2, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA 021266/S-047 VFEND (voriconazole) tablets, 50 mg and 200 mg
NDA 021267/S-057 VFEND I.V. (voriconazole) for injection, 200 mg
NDA 021630/S-036 VFEND (voriconazole) for oral suspension, 40 mg/mL

These Prior Approval supplemental new drug applications provide for revisions to the following sections of the Prescribing Information (PI):

- 1) **HIGHLIGHTS OF PRESCRIBING INFORMATION**, under **RECENT MAJOR CHANGES**, Contraindications (4) and Warnings and Precautions (5.8) have been added. Updates have also been made to **DOSAGE FORMS AND STRENGTHS**, under *For Oral Suspension*, to **CONTRAINDICATIONS** regarding use with naloxegol, and in **WARNINGS AND PRECAUTIONS** information added regarding *Adrenal Dysfunction*.
- 2) **FULL PRESCRIBING INFORMATION, CONTRAINDICATIONS (4)** section, addition of contraindication when coadministered with naloxegol;
- 3) **FULL PRESCRIBING INFORMATION, WARNINGS AND PRECAUTIONS (5)** section, addition of an **Adrenal Dysfunction (5.8)** subsection;
- 4) **FULL PRESCRIBING INFORMATION, ADVERSE REACTIONS (6)** section, **Postmarketing Experience in Adult and Pediatric Patients (6.2)** subsection, addition of an *Endocrine disorders* subheading and information regarding adrenal insufficiency and Cushing's syndrome;
- 5) **FULL PRESCRIBING INFORMATION, DRUG INTERACTIONS (7)** section, **Effect of Voriconazole on Pharmacokinetics of Other Drugs (Table 11)**, addition of information regarding the interaction between voriconazole and naloxegol, prednisolone and other corticosteroids, and ivacaftor;
- 6) **FULL PRESCRIBING INFORMATION, CLINICAL PHARMACOLOGY (12)** section, **Pharmacokinetics (12.3)** subsection, under the Drug Interaction Studies, **Effects of**

Voriconazole on Other Drugs subheading, addition of *Naloxegol* (CYP3A4 substrate) information.

- 7) **FULL PRESCRIBING INFORMATION, DOSAGE FORMS AND STRENGTHS (3)** section and **HOW SUPPLIED/STORAGE AND HANDLING (16)** section, **How Supplied (16.1)** subsection, revisions to the description of the Powder for Oral Suspension;

Additionally, the text under the following sections of the Patient Package Insert (PPI) have been updated to be consistent with the changes made in the PI:

- **Do not take VFEND if you:**
- **Before you take VFEND, tell your healthcare provider about all of your medical conditions, including if you:**
- **What are possible side effects of VFEND? VFEND may cause serious side effects including:**
- **The most common side effects of VFEND in children include:**

Further, a “**bone problems**” subsection has been added to the PPI and minor editorial revisions have been made throughout labeling.

APPROVAL & LABELING

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

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 FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, Instructions for Use), with the addition of any labeling changes in pending “Changes Being Effectuated” (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 *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, 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 Microsoft Word format, that includes the changes approved in these supplemental applications, as well as annual reportable changes.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

To facilitate review of your submission(s), 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

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

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 labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

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 Alison Rodgers, Regulatory Project Manager, at 301-796-0797.

Sincerely,

{See appended electronic signature page}

Dmitri Iarikov, MD, PhD
Deputy Director
Division of Anti-Infectives
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert
 - Instructions for Use

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DMITRI IARIKOV
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