NDA 019949/S-072
NDA 019950/S-071
NDA 020090/S-053

SUPPLEMENT APPROVAL

Pfizer Inc.
Attention: Mikhail Abarshalin
Director
Pfizer Global Regulatory Strategy
66 Hudson Boulevard East
New York, NY 10001

Dear Mikhail Abarshalin:

Please refer to your supplemental new drug applications (sNDAs) dated and received November 8, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA 019949/S-072 Diflucan (fluconazole) Tablets, 50 mg, 100 mg, 150 mg, 200 mg
NDA 019950/S-071 Diflucan (fluconazole in Dextrose Injection and fluconazole in Sodium Chloride Injection, for intravenous use)
NDA 020090/S-053 Diflucan (fluconazole) for Oral Suspension, 350 mg, 1400 mg

These Prior Approval sNDAs provide for updates to the Prescribing Information (PI) with pediatric information in response to our June 13, 2021, supplement request letter in accordance with Section 4091 of the Best Pharmaceuticals for Children Act. The revisions are outlined below:

1) **CLINICAL PHARMACOLOGY** section**, Pharmacokinetics and Metabolism** subsection: Addition of Table 1, Mean Pharmacokinetic Parameters of Fluconazole in Adult Healthy Volunteers Following the Administration of DIFLUCAN.
   a. **Pharmacokinetics in Pediatric Patients** subsection: Revision of Table 3 to add one more row for pediatric patients aged 2 to 60 days and revised footnotes. Following Table 3, text describing pharmacokinetics in pediatric patients (preterm and term infants) and pediatric patients aged birth to 17 years is added.
   b. **Drug Interaction Studies (See PRECAUTIONS, Drug Interactions)** subsection**:** Updated text regarding Voriconazole and added new text for Abrocitinib to align with previously approved (January, 2023) PI.
2) **CLINICAL STUDIES** section**, Pediatric Studies** subsection**:** Referenced age range changed from 6 months to 14.5 years of age to 6 months to 13 years of age.

3) **PRECAUTIONS** section**, General** subsection**:** Addition of Special care information regarding reports of cases of superinfection with *Candida species* other than *C. albican*s.
   a. **Drug Interactions** subsection**:** Addition of text for Abrocitinib to align with the PI approved January 2023.
   b. **Pediatric Use** subsection: Addition of subheadings, "Use in Pediatric Patients for the Treatment of Oropharyngeal Candidiasis," "Use in Pediatric Patients for the Treatment of *Candida* Esophagitis, Systemic *Candida* Infections, or Cryptococcal Meningitis" and "Use in Pediatric Patients on Extracorporeal Membrane Oxygenation (ECMO)." Addition of Tables 4 : "Death or Candidiasis by Day 49 in Premature Infants Receiving DIFLUCAN Prophylaxis" and 5 , "Serious Adverse Reactions* Occurring in >5% of Infants Receiving DIFLUCAN Prophylaxis."
4) **ADVERSE REACTIONS** section**, Adverse Reactions in Pediatric Patients** subsection: Addition of subheading "*Clinical Trials Experience in Pediatric Patients,*" and subsub headings "Safety in Prophylaxis of Invasive *Candida* Infections in Premature infants weighing less than 750 grams at birth" and "Safety in Pediatric Patients Receiving ECMO" with text describing the pediatric studies."
5) **DOSAGE AND ADMINISTRATION** section**, *Dosage and Administration in Pediatric Patients*** subsection**:** Updated age ranges for studies in pediatric patients. *Systemic Candida infections* subheading: Addition of Table 6: Recommended Dosing Regimens for the treatment of Systemic *Candida* Infections in Pediatric Patients, and addition *of "Dosing in Pediatric Patients on ECMO"* subheading and corresponding text.
6) **HOW SUPPLIED** section: Updated storage conditions to add corresponding Fahrenheit values in parenthesis.

Additionally, minor editorial revisions have been made throughout the PI.
The Patient Information for Diflucan Tablets was updated to align with the changes made to the PI.

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 and Patient Information), 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 *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 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 Microsoft Word format, that includes the changes approved in these supplemental applications, as well as annual reportable changes. 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).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

[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.

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, Senior 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 Information

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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