VFEND Pediatric Efficacy Supplement Resubmission

Supporting Document Number:	**NDA 21-266/S-039 (VFEND Oral Tablets)** **NDA 21-267/S-050 (VFEND Intravenous Injection)** **NDA 21-630/S-029 (VFEND Oral Suspension)**
Applicant:	PF Prism C.V.--Pfizer Inc.
Product:	VFEND (Voriconazole) Oral Tablets; Intravenous; Injection; Oral Suspension
Submission Type:	**Pediatric Efficacy Supplements** **Complete Response Resubmission**
CDER Submission Date:	November 29, 2018
CDER Receipt Date:	November 29, 2018
Date Review Completed:	January 22, 2019
Clinical Reviewer, Acting:	Caroline J. Jjingo, MD, MPH, DAIP/OND
Clinical Team Leader:	Yuliya Yasinskaya, MD, DAIP/OND
Regulatory Project Manager:	Alison Rodgers, DAIP/OND
Materials Reviewed:	1. Cover Letter; 2. FPI 3. Rationale and justification document for the proposed labeling changes

Background History:
On June 1, 2017, the Applicant, Pfizer, submitted pediatric efficacy supplements (sNDAs) under the following NDAs and formulations for the drug product VFEND (voriconazole):

- NDA 21-266; SDN-893 (S-039) for VFEND oral tablets;
- NDA 21-267; SDN-512 (S-050) for VFEND IV for injection; and
- NDA 21-630; SDN-273 (S-029) for VFEND oral suspension.

Collectively, these pediatric efficacy supplements proposed to update the VFEND label to include information pertaining to voriconazole dosage and administration and safety in pediatric patients ages 2 to <12 years old. The submission included safety data from 105 patients enrolled in two uncontrolled Phase 3 pediatric studies in patients 2 to <18 years of age (Study A1501080 and Study A1501085) as well as previously collected safety information from patients 12 to <18 years of age enrolled in the original registrational trials.

The Agency issued a complete response (CR) to the Applicant on November 30, 2017 as agreement was not reached on labeling, (b) (4) [redacted] (b) (4) in Table 8 [redacted] ” under **Section 6** Adverse Reactions (sub-section 6.1 “Clinical Trials Experience in Pediatric Patients.”)

Complete Response Resubmission
On November 11, 2018 in their sNDA resubmission, the Applicant provided a complete response to the Agency’s CR letter. Whereas, under Subsection 6.1 “Clinical Trials Experience in Pediatric Patients,” the Agency originally proposed that all pooled, all causality Treatment

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Emergent Adverse Reactions (TEARs) be included in Table 8, the Applicant counter-proposed that [redacted], be included in Table 8, [redacted]. The agreed upon Table 8 is included in the attachment to this review.

Additional Revisions to the Labeling

Dosing VFEND in Adults and Pediatric Patients with Hepatic and Renal Impairments
The following statements on Hepatic and Renal impairment were removed from the [redacted] and included under the "DOSAGE and ADMINSTRATION" section of the HLs.

- *Hepatic impairment*: Use half the maintenance dose in patients with mild to moderate hepatic impairment (Child-Pugh Class A and B) (2.5)

- *Renal impairment*: Avoid intravenous administration in patients with creatinine clearance <50 mL/min (2.6)

Whereas, the following statement was included in the "DOSAGE and ADMINSTRATION" section of the HLs for pediatric patients with hepatic and renal impairments:

- Dosage adjustment of VFEND in pediatric patients with renal or hepatic impairment has not been established (2.5, 2.6)

Conclusion and Recommendations: This reviewer recommends approval of the above listed voriconazole pediatric efficacy supplements as well as the accompanying agreed upon labeling changes.

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/s/

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