NON-INTERVENTIONAL/LOW-INTERVENTIONAL STUDY TYPE 1 STUDY REPORT ABSTRACT

Title: Evaluation of the effectiveness of additional risk minimisation measures (aRMMs) that aim to reduce the risks of phototoxicity, squamous cell carcinoma (SCC) of the skin and hepatic toxicity in patients receiving voriconazole in the Saudi Arabia.

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Keywords: voriconazole; risk minimisation measures; phototoxicity; squamous cell carcinoma; hepatic toxicity

Rationale and background: Voriconazole (Vfend®) is a broad-spectrum triazole antifungal agent approved in Saudi Arabia for treatment of serious invasive fungal infections—including invasive aspergillosis, candidemia (including fluconazole-resistant strains), and infections caused by Scedosporium and Fusarium spp.—as well as for prophylaxis in high-risk allogeneic HSCT recipients. Phototoxicity, squamous cell carcinoma of the skin, and hepatic toxicity are identified risks in Voriconazole's Risk Management Plan and SPC; to mitigate these, Pfizer implemented aRMMs in February 2023, comprising SPC label updates and a targeted HCP educational programme (HCP Checklist, Q&A Brochure, Patient Alert Card).

Research question and objectives: Overall objective: evaluate the effectiveness of the aRMMs in Saudi Arabia to mitigate phototoxicity, SCC and hepatic toxicity with voriconazole. Specific objectives:

1. Assess HCPs' awareness of the RM tools (Checklist, Q&A Brochure, Alert Card).
2. Assess HCPs' utilization of the RM tools.
3. Assess HCPs' knowledge of phototoxicity, SCC and hepatic toxicity risks.
4. Assess whether HCPs' self-reported risk-mitigation practices align with SPC guidance.

Study design: Non-interventional, cross-sectional, web-based survey of HCPs who had prescribed voriconazole in the previous 12 months and were targeted to receive aRMMs. Data collection continued until 10 complete surveys were obtained or for a maximum of 90 days.

Setting: HCPs across the Central, Eastern and Northern regions of Saudi Arabia were invited by email and/or phone to participate.

Subjects and study size, including dropouts: The target population included all HCPs who were targeted to receive Vfend® aRMM materials within 12 months preceding the survey. An

a priori target of 10 complete responses was set; data collection ceased upon receipt of 10 complete surveys. HCPs unreachable after three contact attempts were excluded.

Variables and data sources: A self-administered online questionnaire Redact Decipher) captured eligibility (consent; ≥1 voriconazole patient in past 12 months; non-affiliation; no prior qualitative research), HCP demographics (location, specialty, years in practice, patient load), risk-knowledge (phototoxicity, SCC, hepatic toxicity and discontinuation guidance), aRMM tool receipt/reading/utilization/usefulness, self-reported mitigation practices (sun protection, liver-function monitoring, dermatology referral, SPC-aligned discontinuation), and requests/downloads of materials .

Results: Ten HCPs participated; 6 (60%) clinical pharmacists, 3 (30%) infectious disease physicians, 1 (10%) other; 5 (50%) had 6–15 years' and 5 (50%) >15 years' experience, managing 1–5 patients (50%), 6–10 (20%), 11–20 (20%) and >20 (10%) in the prior year. The receipt of materials was 50% for the Q&A Brochure (20% read fully, 40% partly), 20% for the Checklist (100% read some), and 30% for the Alert Card (33.3% read fully, 66.7% partly); 10% downloaded online. Utilization: 33.3% always and 66.7% sometimes used the Checklist; 60% sometimes and 40% never used the Brochure; among Alert Card recipients, 50% sometimes and 50% never used it. Knowledge was high for phototoxicity (90%) and hepatic toxicity (80%) but lower for SCC (50%), with occasional misclassification of unrelated risks. In practice, 80% advised sun protection, 90% emphasized serious-risk monitoring (including liver damage), 50% recommended systematic dermatologic evaluation, 50% performed liver-function tests at initiation and weekly for 1 month (70% ongoing monthly), and 80% would discontinue voriconazole for key risk factors.

Discussion: Engagement with aRMMs was suboptimal: only half of HCPs received the Q&A Brochure and fewer received the Checklist or Alert Card, and SCC risk awareness remained low, mirroring EU findings. The small, self-selected sample, potential biases, lack of baseline and patient-outcome data, and reliance on self-report limit interpretation. To strengthen Vfend®'s benefit–risk profile, integrated digital reminders, targeted CME and real-world data audits are recommended to reinforce tool uptake and safe-use practices. Voluntary participation and digital access constraints may limit generalizability. Maintaining all aRMM components while piloting streamlined, data-driven interventions could close knowledge gaps and optimise risk minimisation for voriconazole.

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