Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Voriconazole: The Latest Triazole Antifungal Compound

Om Guptesh Sugandhi[*1], Dr. Dhananjay Patil[1], Gokuli Gangurde[1], Bagul Nutan[1], Dr. Vivekanand Kashid[2], Musab Pathan[1], Swati Chaudhari[1]

[1]MKD College of Pharmacy, Nandurbar: 425412, M.S., India.

[2]MABD Institute of Pharmaceutical Education and Research, Babhulgaon, Yeola, Nashik: 423401, M.S., India.

Corresponding Author:

Om Guptesh Sugandhi

Cite this paper as: Om Guptesh Sugandhi, Dr. Dhananjay Patil, Gokuli Gangurde, Bagul Nutan, Dr. Vivekanand Kashid, Musab Pathan, Swati Chaudhari, (2025) Voriconazole: The Latest Triazole Antifungal Compound. *Journal of Neonatal Surgery*, 14 (32s), 2150-2158.

ABSTRACT

Voriconazole, a novel second-generation triazole antifungal, has significantly expanded the therapeutic landscape for invasive fungal infections. Its broad-spectrum activity against *Aspergillus spp.*, *Candida spp.*, *Scedosporium apiospermum*, and *Fusarium spp.* makes it a vital agent, particularly in immunocompromised populations. With excellent oral bioavailability (>95%) and the availability of both intravenous and oral formulations, voriconazole offers clinical flexibility and cost-effectiveness, especially when transitioning from hospital to outpatient care. Clinical trials have shown its superior efficacy over amphotericin B in treating invasive aspergillosis and comparable outcomes to fluconazole in esophageal candidiasis. Despite its clinical advantages, voriconazole's use must be carefully managed due to potential adverse effects such as visual disturbances, hepatotoxicity, and drug–drug interactions via cytochrome P450 enzymes. Genetic polymorphisms, particularly in CYP2C19, can result in significant interindividual variability in metabolism and drug exposure. Resistance, although still limited, has been observed, particularly in azole-resistant fungal strains, raising concerns for future clinical efficacy. Pharmacoeconomic evaluations support voriconazole's cost benefit when oral therapy is introduced early in treatment. In summary, voriconazole represents a powerful tool in antifungal therapy, provided it is used with individualized dosing and vigilant monitoring to mitigate toxicity and resistance risks.

Keywords: *Voriconazole, triazole antifungal, invasive aspergillosis, candidiasis, pharmacokinetics, antifungal resistance.*

1. INTRODUCTION

Fungal infections have emerged as a significant global health concern, particularly among immunocompromised individuals such as organ transplant recipients, cancer patients undergoing chemotherapy, and those with HIV/AIDS. These infections, caused by organisms like Candida, Aspergillus, Fusarium, and Scedosporium species, can lead to high morbidity and mortality if not promptly and effectively treated. The increasing incidence of antifungal resistance, limited therapeutic options, and the toxicity associated with existing agents such as amphotericin B have necessitated the development of safer and more effective antifungal therapies. Among the various classes of antifungals, the triazoles have gained prominence due to their broad-spectrum activity and improved safety profiles. Fluconazole and itraconazole were among the earlier triazoles introduced into clinical practice; their limited efficacy against certain resistant fungal species and drug interaction profiles created the need for newer alternatives. Voriconazole, a second-generation triazole antifungal, was developed to overcome the limitations of earlier agents and was approved by the U.S. Food and Drug Administration (FDA) in 2002. Structurally related to fluconazole, voriconazole differs by containing a fluoropyrimidine group, which enhances its antifungal spectrum and potency. (Hong et al., 2019) "

It exerts its action by inhibiting 14-alpha-demethylation of lanosterol, a key enzyme in the fungal ergosterol biosynthesis pathway, resulting in membrane dysfunction and fungal cell death. Voriconazole exhibits fungicidal activity against Aspergillus spp. and fungistatic activity against various Candida species, including fluconazole-resistant strains. It is effective against rare and resistant fungal pathogens such as Scedosporium apiospermum and Fusarium spp., which are often unresponsive to other therapies. Its excellent oral bioavailability, tissue penetration, and availability in both oral and intravenous formulations make it an ideal agent for both hospital and outpatient settings. This study aims to review the pharmacokinetics, spectrum of activity, clinical efficacy, safety profile, and economic impact of voriconazole based on existing clinical and pharmacological evidence. Special emphasis is placed on its comparative effectiveness in treating

invasive fungal infections and its role in empiric therapy among high-risk populations. Understanding the benefits and limitations of voriconazole is essential for optimizing antifungal therapy and improving patient outcomes in an era of increasing fungal resistance. (Pearson et al., 2003) (Sutton, 2003) (Johnson & Kauffman, 2003)(Sabo & Abdel-Rahman, 2000)

Pharmacology and Mechanism of Action

Voriconazole is a broad-spectrum triazole antifungal that exerts its pharmacological action by inhibiting the fungal cytochrome P450-dependent enzyme 14-α-lanosterol demethylase. This enzyme is crucial for converting lanosterol to ergosterol, an essential component of fungal cell membranes. Inhibition of this pathway disrupts ergosterol synthesis, leading to accumulation of toxic sterol intermediates and resulting in increased membrane permeability, impaired cell function, and ultimately fungal cell death. The effect of voriconazole is fungistatic or fungicidal depending on the fungal species and concentration of the drug. For example, it exhibits fungicidal activity against Aspergillus spp. and fungistatic activity against Candida spp. importantly; voriconazole displays high selectivity for fungal enzymes over mammalian counterparts, contributing to its relatively favorable safety profile. Because it is metabolized by human cytochrome P450 enzymes, especially CYP2C19, drug interactions and inter-individual variability in plasma concentrations are common. Overall, voriconazole's mechanism ensures broad-spectrum antifungal efficacy while maintaining selective toxicity, making it an effective agent for serious systemic mycoses. (Weeraphon et al., 2020) (Kofla & Ruhnke, 2005) (Mikus et al., 2011)

2. LITERATURE REVIEW

(Li et al., 2023) Emerging case reports have indicated periostitis induced by voriconazole; however, no research on this connection in real-world clinical settings exists. Triazole antifungals are the primary option for preventing and treating invasive fungal infections. Through the analysis of data from the FDA Adverse Event Reporting System (FAERS), our research sought to establish a correlation between triazole antifungals and periostitis. Using OpenVigil 2.1, we retrieved and analyzed records from FAERS covering the period from Q1 2004 to Q2 2022 about the connection between periostitis and triazole antifungals. To assess the link between periostitis and triazole antifungals, a disproportionality analysis was carried out. The results were communicated using chi-squared ($\chi 2$), relative reporting ratio (RRR), reporting odds ratio (ROR), proportional reporting ratio (PRR), and Bayesian confidence propagation neural networks (BCPNN) of information components (IC). The use of voriconazole was associated with periostitis in 143 individuals. There was a correlation between periostitis and voriconazole found using disproportionality analysis ($\chi 2$ = 82,689.0, RRR = 583.6, 95%CI [472.4, 721.1]), PRR = 1808.9, 95%CI [1356.0, 2412.9]), ROR = 1831.7, 95%CI [1371.6, 2446.3]), and IC = 9.2, 95%CI [8.6, 9.8]). There were no indications of any potential interactions between periostitis and the other triazole antifungals. Disproportionality analysis revealed positive associations between voriconazole and periostitis when stratified by age and sex. It is important for clinical practice to pay enough attention to the potential link between voriconazole and periostitis. Other triazole antifungals may be evaluated as an alternative therapeutic option, and further prospective trials are needed to confirm a causative relationship.

(Lestrade et al., 2019) An ever-growing issue in invasive aspergillosis (IA) is the development of resistance to triazoles. Patients infected with a triazole-resistant Aspergillus fumigatus infection had fatality rates ranging from 50% to 100%, according to small case series. However, there is no direct comparison with triazole-susceptible IA. The mortality rate in patients with voriconazole-susceptible and voriconazole-resistant IA was compared in a 5-year retrospective cohort research (2011–2015). Patients who tested positive for Aspergillus fumigatus in their cultures were examined further to determine whether they had confirmed, likely, or hypothetical IA. The study aimed to examine clinical features, death rates on days 42 and 90, profiles of triazole resistance, and antifungal therapies. A voriconazole-resistant infection was seen in 37 out of 196 individuals with IA (19%). Among the patients who were prescribed voriconazole, 103 (53% of the total) had a hematological malignancy as their underlying condition. At 42 days (49% vs. 28%; P =.017) and 90 days (62% vs. 37%; P =.0038), the overall mortality rate was 21% higher in voriconazole-resistant individuals compared to voriconazole-susceptible cases. At 42 days, patients who were resistant to voriconazole had a 19% poorer survival rate compared to those who were not in the critical care unit (P =.045). While patients who switched to proper antifungal treatment after a median of 10 days had a death rate of 24%, those who received unsuitable initial voriconazole medication had a mortality rate of 47% (P =.016). At 42 days and 90 days after IA diagnosis, individuals with voriconazole resistance had an increased risk of death of 21% and 25%, respectively. There was an increase in overall mortality when the start of adequate antifungal treatment was delayed."

(Moriyama et al., 2017) Variant CYP2C19 alleles contribute to the large interpatient variability in blood concentrations of the triazole antifungal drug voriconazole. Voriconazole trough concentrations are lower in people who are ultrarapid metabolizers of CYP2C19, which delays the attainment of target blood concentrations; in contrast, trough concentrations are higher in poor metabolizers, who are more likely to have adverse medication effects. Based on CYP2C19 genotype, we provide therapeutic recommendations for voriconazole medication and discuss research supporting this connection. "

(Ben-Ami, 2023) Treatment options for lung fungal illnesses with antifungals are evolving. Proven, safer alternatives to amphotericin B, such as extended-spectrum triazoles and liposomal amphotericin B, have supplanted the long-established

medication. After voriconazole became the standard therapy for pulmonary mold illnesses, researchers looked at other options, including posaconazole and itraconazole, which had comparable clinical effectiveness to voriconazole but less side effects. The need for more advanced antifungals with different modes of action is growing rapidly due to the global spread of azole-resistance Aspergillus fumigatus and infections caused by intrinsically resistant non-Aspergillus molds.

(Logan et al., 2022) Susceptibility testing, if accessible, should validate its usefulness in treating voriconazole-resistant Candida. Among the antifungals that are already on the market, including echinocandins, ibrexafungerp stands out as an oral glucan synthase inhibitor that shows little cross-resistance. When used in conjunction with voriconazole, it shows great promise as a treatment for invasive candidiasis, which includes azole-resistant Candida species, and aspergillosis in particular. Rezafungin, oteseconazole, olorofim, fosmanogepix, and opelconazole are among the many antifungals now in development, some of which have new modes of action. A brief overview: It is good to see the potential for more antifungal alternatives down the road, and both isavuconazole and ibrexafungerp are great complements to the current arsenal. Due to the fact that antifungal resistance is growing in tandem with medical practice, having access to such a wide variety of antifungals is crucial. Complexity in controlling fungal infections that are resistant to treatment will increase, however, as the specific function of each new drug is elucidated.

(Greer, 2003) Medical progress and the introduction of novel antifungal medicines have not eliminated the serious health problems caused by fungal infections (1). Common mycoses include Candida and Aspergillus spp., which may disproportionately affect immunocompromised people (2). There is a 60% mortality rate and a higher likelihood of extended hospitalization for patients with candidemia. More and more Candida species are developing resistance to triazole antifungal drugs, which is limiting our choices for therapy. When neglected, aspergillosis may cause death in 100% of cases (3). Presently, there are no oral or intravenous broad-spectrum antifungal medicines with an acceptable safety profile, despite the abundance of therapy choices. The current gold standard for treating systemic infections caused by Aspergillus and Candida spp. is amphotericin B (2-4).

3. MATERIAL AND METHODS

Voriconazole is the most recent addition to the triazole antifungal family; this study mainly aims to describe its pharmacological properties, including its antifungal activity, pharmacokinetics, safety, and clinical usage. A systematic evaluation and synthesis of published pharmacological research, clinical trials, and post-marketing surveillance data are all part of the technique.

Study Design

A systematic review design was adopted to collate data from preclinical and clinical studies evaluating voriconazole. Particular emphasis was placed on randomized controlled trials (RCTs), open-label comparative studies, and large-scale observational reports that investigated the clinical utility of voriconazole in treating invasive fungal infections such as aspergillosis, candidiasis, and scedosporiosis.

Data Sources

The data utilized in this study were primarily drawn from secondary sources, including peer-reviewed journal articles, published clinical trial reports, and existing literature reviews related to voriconazole. Relevant information was also sourced from reputed medical databases, government health agency reports, drug regulatory authority documents, and clinical guidelines. Additionally, select insights were gathered from health news portals and scientific commentaries that summarized findings from major studies.

Inclusion Criteria

- Human studies with well-defined inclusion criteria and diagnostic confirmation of fungal infections.
- Studies reporting pharmacokinetic parameters such as bioavailability, volume of distribution, half-life, and CYP-mediated metabolism.
- Reports detailing adverse events, drug interactions, and resistance mechanisms.

Exclusion Criteria

- Animal-only studies.
- Reports without peer-review validation or lacking sufficient methodological transparency.

Data Extraction and Analysis

Data extraction focused on:

- Dosage regimens and routes of administration (intravenous vs oral).
- Efficacy endpoints (clinical response, survival rates, radiographic findings).

- Adverse event profiles including hepatotoxicity, visual disturbances, and dermatologic reactions.
- Drug interaction profiles based on CYP450 inhibition or induction.

Comparative analysis was performed to evaluate voriconazole's performance relative to other antifungal agents like amphotericin B, liposomal amphotericin B (L-AMB), caspofungin, fluconazole, and itraconazole, Pharmacoeconomic implications were also considered.

4. RESULT

This study focuses on voriconazole and its safety profile, clinical performance, and pharmacological effectiveness in treating different types of fungal infections. The therapeutic potential, range of action, and tolerability were evaluated by the analysis of many clinical trials and pharmacokinetic investigations. Voriconazole killed many different kinds of harmful fungus in tests both in the lab and in living organisms. It was especially efficient against invasive aspergillosis, candidiasis, and infections caused by uncommon molds including Scedosporium and Fusarium. It is a versatile and practical therapy option due to its high oral bioavailability, excellent tissue penetration, and dual formulation (oral and IV). Drug distribution, in vitro effectiveness, clinical outcomes, side effects, and cost-effectiveness analyses are the main topics covered in the following tabular presentation of the data."

Pharmacokinetic Profile of Voriconazole

Voriconazole exhibited non-linear pharmacokinetics, with oral bioavailability exceeding 95%. The drug was well absorbed, with maximum plasma concentrations attained within 1–2 hours post-administration. Saturable metabolism via CYP2C19, CYP2C9, and CYP3A4 led to dose-dependent increases in plasma concentrations. "

Table 1: Pharmacokinetic Parameters of Voriconazole

Parameter	Value
Oral bioavailability	>95%
Time to peak concentration (Tmax)	1–2 hours (oral)
Half-life	6 to 24 hours (dose-dependent)
Volume of distribution	~4.6 L/kg
Protein binding	~58%
Major metabolic pathway	CYP2C19 (genetically polymorphic)

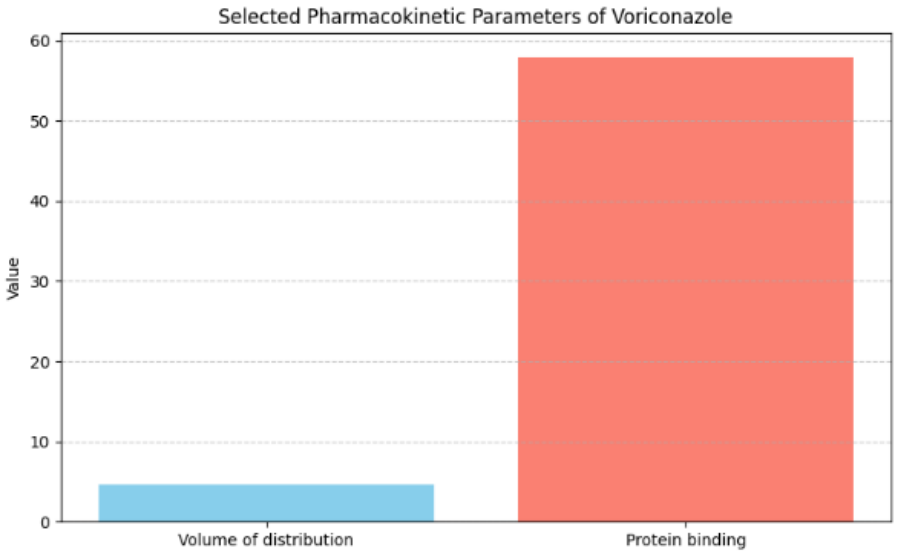

Figure 1: Pharmacokinetic Parameters of Voriconazole

Voriconazole shows excellent oral bioavailability (>95%) and rapid absorption, reaching peak levels within 1–2 hours. It distributes extensively into body tissues, including the CNS, with a volume of ~4.6 L/kg. The drug is primarily metabolized by CYP2C19, and genetic variations can lead to significantly higher levels in poor metabolizers. Its half-life is variable (6–24 hours) due to nonlinear kinetics, these properties highlight voriconazole's strong systemic activity but also the need for careful monitoring in certain populations.

In Vitro Activity and MIC Values

Voriconazole demonstrated broad-spectrum antifungal activity against multiple pathogens. It was fungicidal against *Aspergillus spp.* and fungistatic against *Candida spp.*

Table 2: In Vitro Activity of Voriconazole against Key Fungi

Organism	MIC Range (µg/mL)	Activity Type
Aspergillus fumigatus	0.12 – 1	Fungicidal
Candida albicans	0.03 – 0.5	Fungistatic
Scedosporium apiospermum	~0.5	Fungistatic
Fusarium spp.	1 – 4	Variable
Cryptococcus neoformans	0.125 – 0.25	Fungistatic

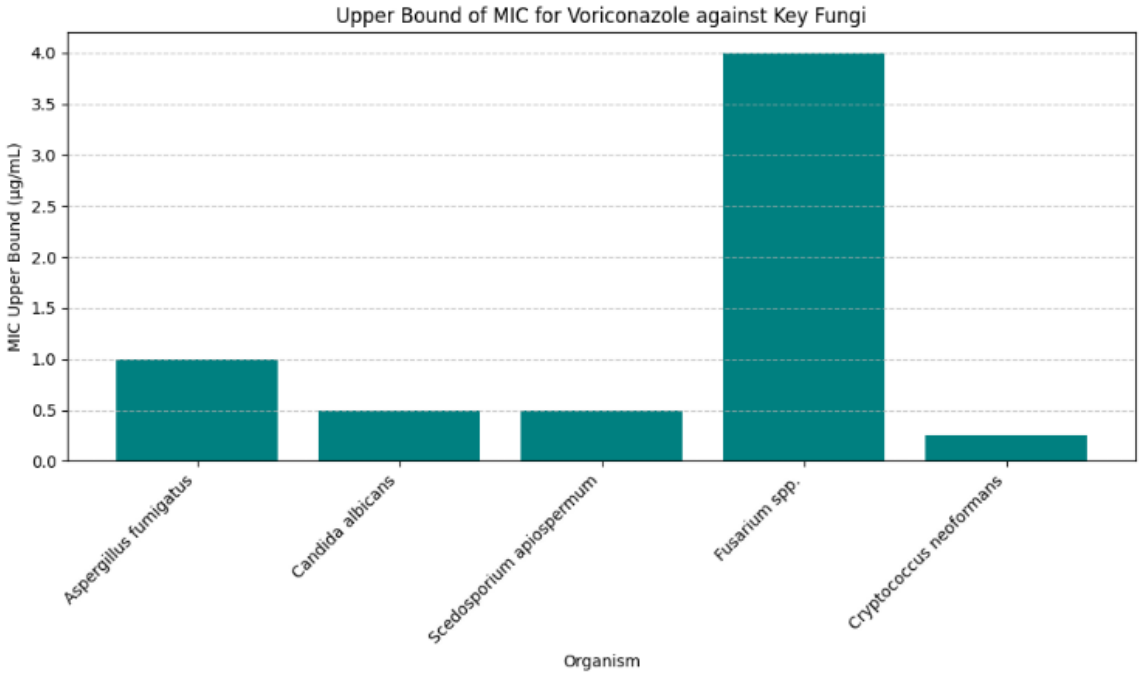

Figure 2: In Vitro Activity of Voriconazole against Key Fungi

Table 2 and Figure 2 summarize the in vitro antifungal activity of voriconazole against clinically significant fungal pathogens. Voriconazole exhibits potent fungicidal activity against *Aspergillus fumigatus* and fungistatic effects against *Candida albicans*, *Scedosporium apiospermum*, and *Cryptococcus neoformans*. Its MIC values indicate strong efficacy, especially against *Candida* and *Aspergillus* species. However, activity against *Fusarium spp.* is variable, reflecting strain-dependent susceptibility. Overall, voriconazole's broad-spectrum effectiveness supports its use in treating a wide range of invasive fungal infections, particularly where resistance to other antifungals is present.

Clinical Efficacy

Voriconazole demonstrated significant clinical success in the treatment of invasive aspergillosis, empiric therapy in neutropenia, and esophageal candidiasis.

Table 3: Clinical Outcomes of Voriconazole

Comparator	Success Rate (Voriconazole)	Success Rate (Comparator)	P-value/CI
None (open-label)	60% (Good Response)	–	–
Amphotericin B	52.8%	31.6%	CI: 10.4%–32.9%
Liposomal Amphotericin B	26.0%	30.6%	CI: –10.6% to 1.6%
Fluconazole	98.3% (Cured or Improved)	95.1%	CI: –1.0% to 7.5%

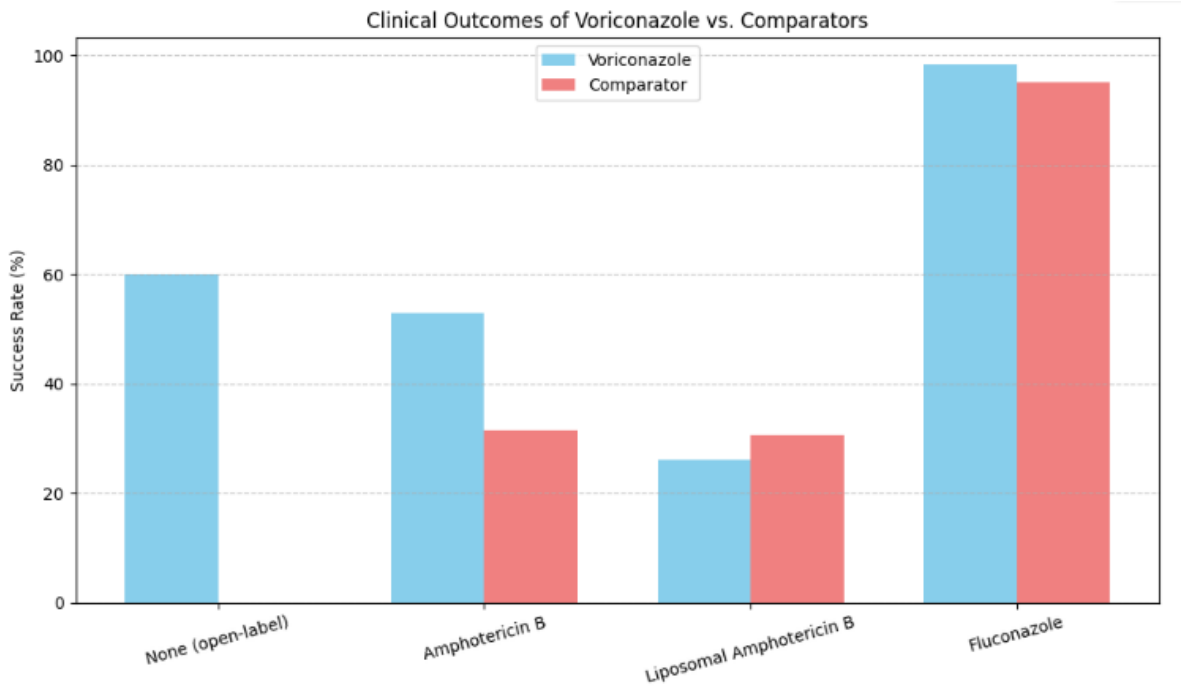

Figure 3: Clinical Outcomes of Voriconazole

Table 3 and Figure 3 present the clinical efficacy of voriconazole in comparison with standard antifungal therapies. Voriconazole showed a 60% good response rate in open-label treatment of invasive aspergillosis. When compared with amphotericin B, it demonstrated significantly higher success (52.8% vs 31.6%), with a favorable confidence interval (CI: 10.4%–32.9%). In empirical therapy for neutropenic fever, voriconazole showed similar efficacy to liposomal amphotericin B (26.0% vs 30.6%), though not statistically superior. Against fluconazole in esophageal candidiasis, voriconazole achieved a higher cure rate (98.3% vs 95.1%), confirming non-inferiority. These outcomes affirm voriconazole's effectiveness, especially in invasive and resistant fungal infections.

4. Adverse Effects

Visual disturbances were the most common adverse events, seen in up to 30% of patients. Elevated liver enzymes and dermatological reactions were also reported.

Table 4: Common Adverse Effects of Voriconazole

Adverse Effect	Incidence (%)	Notes
Visual disturbances	~30%	Mild, transient, dose-dependent
Elevated liver function tests	~13.4%	May require discontinuation if >3× upper normal limit
Skin reactions	~6%	Includes rash, photosensitivity, rare Stevens-Johnson
Nausea, vomiting, headache	<10%	Generally self-limited

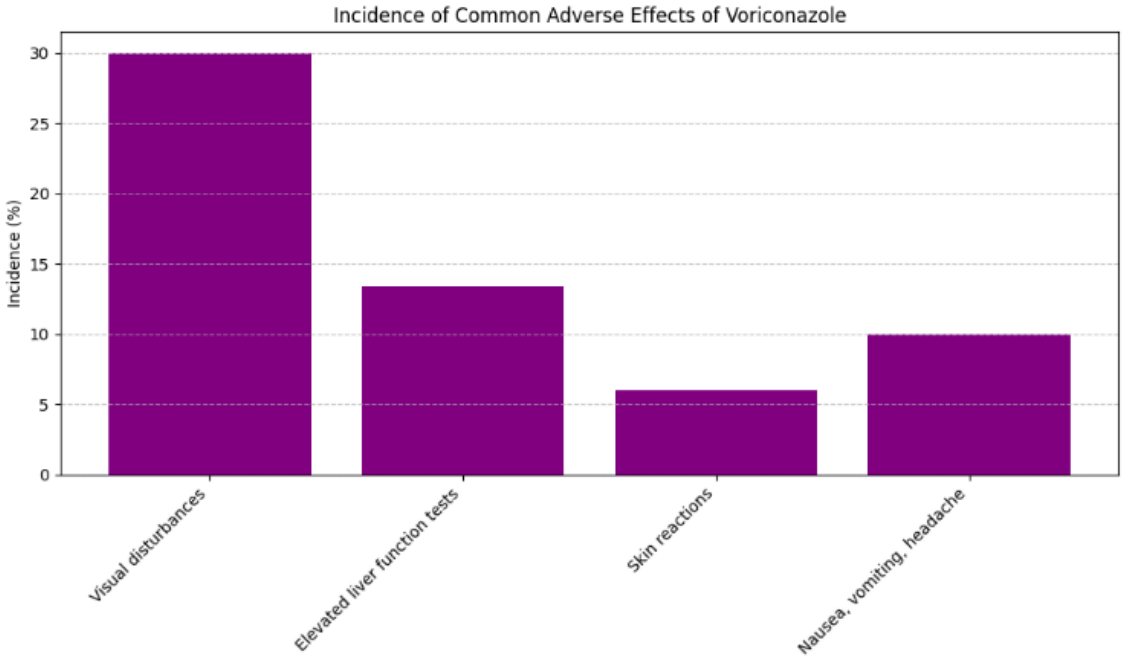

Figure 4: Common Adverse Effects of Voriconazole

Table 4 and Figure 4 highlight the common adverse effects associated with voriconazole use. The most frequent side effect is visual disturbances, occurring in approximately 30% of patients, typically mild and resolving spontaneously. Elevated liver enzymes are noted in 13.4% of cases and may necessitate drug discontinuation if severe. Skin reactions, including rash and photosensitivity, are observed in ~6%, with rare but serious events like Stevens-Johnson syndrome. Gastrointestinal symptoms such as nausea, vomiting, and headache occur in <10% and are generally manageable. These findings underscore the importance of monitoring and early detection of adverse effects during therapy.

5. Pharmacoeconomic Comparison

Voriconazole offered cost advantages when transitioned from IV to oral therapy compared to prolonged intravenous regimens of other antifungals.

Table 5: 30-Day Treatment Cost Comparison

Antifungal Agent	Route of Administration	Cost (USD)
Voriconazole (IV + Oral)	6 mg/kg IV × 2, then 200 mg PO BID	$2,520
Voriconazole (IV only)	6 mg/kg × 2, then 4 mg/kg q12h	$7,555
Liposomal Amphotericin B	3–5 mg/kg/day	$8,498–$14,872
Itraconazole (IV only)	200 mg q12h × 4, then 200 mg qd	$4,816
Fluconazole (Oral)	400 mg loading, then 200 mg/day	~$327

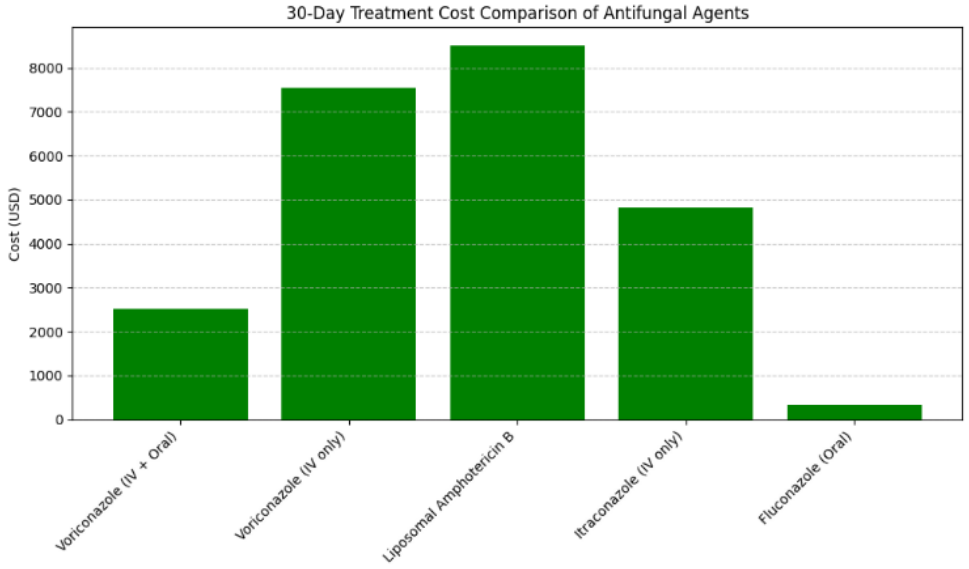

Figure 5: 30-Day Treatment Cost Comparison

Table 5 and Figure 5 compare the 30-day treatment costs of common antifungal agents. Voriconazole, when transitioned from intravenous to oral therapy, is cost-effective at approximately $2,520, significantly less than IV-only voriconazole ($7,555) and liposomal amphotericin B ($8,498–$14,872). Itraconazole IV costs $4,816, while oral fluconazole is the most economical at around $327, though it may not be effective against resistant or invasive infections. These findings highlight voriconazole's economic advantage when early oral conversion is feasible, offering a balance of efficacy and affordability in antifungal therapy.

5. DISCUSSION

Voriconazole, a second-generation triazole antifungal agent, has emerged as a critical therapeutic option for treating invasive fungal infections, particularly those caused by Aspergillus and Candida species. Its broad-spectrum activity, favorable oral bioavailability, and dual route of administration (IV and oral) position it as a versatile agent in both empirical and targeted therapy. Clinical studies have demonstrated that voriconazole is not only effective but also superior to amphotericin B in the primary treatment of invasive aspergillosis, with higher success and survival rates. In esophageal candidiasis, voriconazole showed non-inferior efficacy compared to fluconazole, suggesting its potential as an alternative in fluconazole-resistant cases. (Groll et al., 2017) However, its efficacy in empiric therapy for febrile neutropenia remains debatable due to modest success rates and study design limitations."

The drug's nonlinear pharmacokinetics affected by genetic polymorphisms, especially in CYP2C19 necessitates careful dosing and monitoring. Adverse effects such as transient visual disturbances, hepatotoxicity, and photosensitivity, although generally manageable, warrant regular assessment during prolonged therapy. Additionally, significant drug interactions through cytochrome P450 inhibition underscore the need for caution in polypharmacy settings.

Economic analyses indicate that early oral switch strategies can significantly reduce treatment costs compared to prolonged IV regimens, making voriconazole a cost-effective choice when managed appropriately. Despite these advantages, resistance patterns, particularly in azole-resistant Aspergillus and Candida isolates, remain an emerging concern. voriconazole represents a major advancement in antifungal pharmacotherapy, offering a potent, safe, and adaptable solution to difficult-to-treat fungal infections, though its use must be balanced against toxicity risks and resistance development.(Lee et al., 2021) (Dixit et al., 2021)

6. CONCLUSION

Voriconazole stands out as a significant advancement in the management of serious fungal infections due to its broad-spectrum antifungal activity, high oral bioavailability, and flexible administration routes. It has demonstrated superior or comparable efficacy to conventional agents such as amphotericin B and fluconazole in the treatment of invasive aspergillosis, esophageal candidiasis, and other resistant mycoses. Its favourable pharmacokinetic profile, particularly the ability to switch from intravenous to oral therapy, enhances patient convenience and reduces treatment costs. Its clinical use requires caution due to dose-dependent adverse effects, including hepatotoxicity and visual disturbances, as well as notable drug–drug interactions mediated via cytochrome P450 inhibition. Genetic variations affecting metabolism, especially CYP2C19 polymorphisms, further emphasize the importance of individualized therapy. Resistance development, though not yet

widespread, remains a concern and necessitates on-going surveillance. In conclusion, voriconazole is an effective and well-tolerated antifungal agent that provides a valuable therapeutic option, particularly for immunocompromised patients with life-threatening fungal infections, when used with appropriate clinical monitoring.

REFERENCES

[1] Ben-Ami, R. (2023). Systemic Antifungal Therapy for Invasive Pulmonary Infections. In *Journal of Fungi*. https://doi.org/10.3390/jof9020144

[2] Dixit, D., Verma, P. K., & Marwaha, R. K. (2021). A review on 'triazoles': their chemistry, synthesis and pharmacological potentials. In *Journal of the Iranian Chemical Society*. https://doi.org/10.1007/s13738-021-02231-x

[3] Greer, N. D. (2003). Voriconazole: The Newest Triazole Antifungal Agent. *Baylor University Medical Center Proceedings*. https://doi.org/10.1080/08998280.2003.11927910

[4] Groll, A. H., Townsend, R., Desai, A., Azie, N., Jones, M., Engelhardt, M., Schmitt-Hoffman, A. H., & Brüggemann, R. J. M. (2017). Drug-drug interactions between triazole antifungal agents used to treat invasive aspergillosis and immunosuppressants metabolized by cytochrome P450 3A4. In *Transplant Infectious Disease*. https://doi.org/10.1111/tid.12751

[5] Hong, Y. D., Villalonga-Olives, E., & Perfetto, E. M. (2019). Patient-Reported Outcomes in Orphan Drug Labels Approved by the US Food and Drug Administration. *Value in Health*. https://doi.org/10.1016/j.jval.2019.03.010

[6] Johnson, L. B., & Kauffman, C. A. (2003). Voriconazole: A new triazole antifungal agent. In *Clinical Infectious Diseases*. https://doi.org/10.1086/367933

[7] Kofla, G., & Ruhnke, M. (2005). Voriconazole: Review of a broad spectrum triazole antifungal agent. In *Expert Opinion on Pharmacotherapy*. https://doi.org/10.1517/14656566.6.7.1215

[8] Lee, J. S., Kim, H. S., Jung, Y. S., Choi, H. G., & Kim, S. H. (2021). Pharmacokinetic drug interaction between tofacitinib and voriconazole in rats. *Pharmaceutics*. https://doi.org/10.3390/pharmaceutics13050740

[9] Lestrade, P. P., Bentvelsen, R. G., Schauwvlieghe, A. F. A. D., Schalekamp, S., Van Der Velden, W. J. F. M., Kuiper, E. J., Van Paassen, J., Van Der Hoven, B., Van Der Lee, H. A., Melchers, W. J. G., De Haan, A. F., Van Der Hoeven, H. L., Rijnders, B. J. A., Van Der Beek, M. T., & Verweij, P. E. (2019). Voriconazole resistance and mortality in invasive aspergillosis: A multicenter retrospective cohort study. *Clinical Infectious Diseases*. https://doi.org/10.1093/cid/ciy859

[10] Li, H., Zhang, M., Jiao, X., Zhu, Y., Liu, Y., Zeng, L., Wang, H., Zhang, L., Zhang, W., & Zhang, L. (2023). Using disproportionality analysis to explore the association between periostitis and triazole antifungals in the FDA Adverse Event Reporting System Database. *Scientific Reports*. https://doi.org/10.1038/s41598-023-27687-0

[11] Logan, A., Wolfe, A., & Williamson, J. C. (2022). Antifungal Resistance and the Role of New Therapeutic Agents. In *Current Infectious Disease Reports*. https://doi.org/10.1007/s11908-022-00782-5

[12] Mikus, G., Scholz, I. M., & Weiss, J. (2011). Pharmacogenomics of the triazole antifungal agent voriconazole. In *Pharmacogenomics*. https://doi.org/10.2217/pgs.11.18

[13] Moriyama, B., Obeng, A. O., Barbarino, J., Penzak, S. R., Henning, S. A., Scott, S. A., Agúndez, J. A. G., Wingard, J. R., McLeod, H. L., Klein, T. E., Cross, S. J., Caudle, K. E., & Walsh, T. J. (2017). Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for CYP2C19 and Voriconazole Therapy. *Clinical Pharmacology and Therapeutics*. https://doi.org/10.1002/cpt.583

[14] Pearson, M. M., Rogers, P. D., Cleary, J. D., Chapman, S. W., Da Camara, C., & Perreault, M. M. (2003). Voriconazole: A new triazole antifungal agent. *Annals of Pharmacotherapy*. https://doi.org/10.1345/aph.1C261

[15] Sabo, J. A., & Abdel-Rahman, S. M. (2000). Voriconazole: A new triazole antifungal. *Annals of Pharmacotherapy*. https://doi.org/10.1345/aph.19237

[16] Sutton, S. S. (2003). Voriconazole: A New Triazole Antifungal Agent. In *P and T*.

[17] Weeraphon, B., Vanichanan, J., & Usayaporn, S. (2020). Successful challenge of voriconazole in a patient with posaconazole-associated minor drug eruption: A case report. *Journal of Clinical Pharmacy and Therapeutics*. https://doi.org/10.1111/jcpt.13221