

Terbinafine

Terbinafine is a member of the allylamine class of antifungal medications, primarily used for the treatment of superficial fungal infections. It is available in both oral and topical formulations, offering versatility in managing a variety of dermatological fungal conditions. The topical formulation was approved by the U.S. Food and Drug Administration (FDA) in 1993, while the oral form was approved in 1996. Terbinafine's ability to effectively treat infections of the skin, nails, and scalp has made it a cornerstone in the management of dermatophyte-related diseases, particularly onychomycosis and tinea capitis.

Pharmacokinetics and Metabolism

Terbinafine is well-absorbed when administered orally, with extensive distribution across the body, including the skin, hair, and nails, where it accumulates and remains effective for several months due to its prolonged elimination from these tissues. Following oral administration, approximately 70% of terbinafine is excreted unchanged in the urine, indicating minimal hepatic metabolism in comparison to other antifungal agents. Topical administration of terbinafine, in contrast, leads to localized drug action with minimal systemic absorption, making it suitable for treating superficial skin infections.

Mechanism of Action

Terbinafine exerts its antifungal effects by inhibiting squalene monooxygenase, an enzyme involved in the biosynthesis of ergosterol, a component of the fungal cell membrane. This inhibition results in a reduction of ergosterol levels, impairing fungal cell membrane integrity and hindering fungal growth. Additionally, the accumulation of squalene due to this enzymatic inhibition further disrupts the fungal cell membrane. As a result, terbinafine has a fungicidal effect, particularly effective against dermatophytes. The drug's ability to concentrate in the nails enhances its efficacy in treating onychomycosis, a condition that is otherwise difficult to manage with other antifungal agents.

Clinical Applications

Terbinafine is indicated for the treatment of a variety of dermatophytoses, including:

- **Onychomycosis:** Terbinafine is regarded as the most effective oral treatment for onychomycosis, with cure rates ranging from 50% to 70% (Tosti et al., 2020). Its ability to

penetrate and remain in the nail beds makes it particularly suited for this challenging infection.

- ***Tinea capitis***: Terbinafine is also effective in the treatment of tinea capitis, particularly in children, where it can help eliminate fungal infections of the scalp caused by dermatophytes such as *Trichophyton* species.
- ***Tinea pedis, tinea cruris, and tinea corporis***: The topical formulation is frequently used to treat athlete's foot (*tinea pedis*), ringworm of the body (*tinea corporis*), and jock itch (*tinea cruris*).
- ***Tinea versicolor***: Terbinafine has demonstrated effectiveness against *Malassezia furfur*, the yeast responsible for this superficial skin infection.

Additionally, terbinafine has demonstrated broad antifungal activity against several dermatophytes, including *Epidermophyton*, *Microsporum* and, *Trichophyton* species. However, it is not effective against *Candida* species, limiting its use in infections caused by yeasts.

Adverse Effects and Safety Considerations

While terbinafine is generally well tolerated, it is associated with a range of potential side effects. The most common adverse reactions to oral terbinafine include gastrointestinal symptoms (e.g., nausea, vomiting, dyspepsia), dermatologic reactions (e.g., pruritus, rash, alopecia), and systemic symptoms such as headache, vertigo, and pyrexia. Serious adverse effects, though rare, include hepatotoxicity, Stevens-Johnson syndrome, toxic epidermal necrolysis, anaphylaxis, and blood dyscrasias such as thrombocytopenia and neutropenia.

Oral terbinafine is contraindicated in individuals with hepatic dysfunction or a creatinine clearance of less than 50 mL/min, due to its hepatic metabolism and renal excretion pathways. Special caution is advised for patients with systemic lupus erythematosus (SLE), psoriasis, or immunodeficiency. Baseline liver and renal function tests should be conducted prior to initiating treatment, and ongoing monitoring is recommended for those on long-term therapy, particularly those with pre-existing conditions or immunocompromised patients receiving treatment for longer than six weeks.

Topical terbinafine, in contrast, has a relatively favorable safety profile, with the most common adverse reactions being mild and local, including pruritus, contact dermatitis, burning, stinging, or dryness at the site of application. These side effects are typically transient and resolve after discontinuation of the medication.

Pregnancy and Lactation

Terbinafine should only be used during pregnancy if the benefits to the mother outweigh the potential risks to the fetus. No studies have definitively established its safety in pregnancy, and its use is generally avoided unless absolutely necessary. Terbinafine is contraindicated during lactation, as there is insufficient data to assess its safety in breastfeeding mothers.

Drug Interactions

Terbinafine has the potential to interact with various medications, including *pimozide*, *tricyclic antidepressants*, *cyclosporine*, *rifampin*, and *cimetidine*. These interactions can alter the pharmacokinetics of either terbinafine or the co-administered drugs, leading to enhanced or reduced therapeutic effects or an increased risk of adverse reactions. Monitoring for drug interactions is essential, particularly in patients on many medications.

Conclusion

Terbinafine is a highly effective antifungal agent with broad dermatophyte coverage, making it the treatment of choice for several superficial fungal infections, particularly onychomycosis and tinea capitis. Its mechanism of action, involving inhibition of squalene monooxygenase, leads to a fungicidal effect that disrupts the fungal cell membrane. While terbinafine is generally safe, it does carry the risk of liver toxicity, especially in patients with pre-existing hepatic conditions, and requires careful monitoring. The topical formulation provides an effective and well-tolerated option for managing localized fungal skin infections. Consideration should be given to drug interactions and contraindications, particularly in vulnerable patient populations.

References

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