SAFER Rx
SAFER USE OF HIGH RISK MEDICINES

Waitemata District Health Board
Best Care for Everyone

TERBINAFINE - SAFE PRESCRIBING - NAIL IT

- BE AWARE THAT TERBINAFINE CAN CAUSE SERIOUS ADVERSE REACTIONS
- ADVISE PATIENTS TO REPORT SYMPTOMS OF HEPATOTOXICITY AND ANY SKIN REACTIONS
- ALWAYS CONFIRM PRESENCE OF SUSCEPTIBLE FUNGAL ORGANISMS BEFORE PRESCRIBING
- CONSIDER THE BENEFITS OF TERBINAFINE AGAINST POTENTIAL FOR HARM

Oral terbinafine is indicated for dermatophyte infections of the nails (onychomycosis) and skin where oral therapy is appropriate (eg due to the site, severity or extent of infection).[1] If pharmacological treatment is appropriate, oral terbinafine is usually considered first line [6,7,10] but its use is associated with a number of rare, but potentially serious adverse reactions.[2]

BE AWARE THAT TERBINAFINE CAN CAUSE SERIOUS ADVERSE REACTIONS

The most frequently reported adverse effects associated with oral terbinafine are gastrointestinal including abdominal discomfort, anorexia, nausea and diarrhoea. Rashes (eg urticaria) can also occur, sometimes associated with arthralgia or myalgia.[1] Headache has also been reported in 1-10% of patients.

Serious adverse reactions, although rare, have been linked to terbinafine use. Hepatotoxicity (eg cholestatic jaundice) and dermatological reactions including Stevens-Johnson syndrome and Toxic Epidermal Necrolysis have been reported.[2,4,5] Terbinafine can also cause serious blood dyscrasias, including agranulocytosis and severe neutropenia.[2,4,5]

Liver function tests (LFTs) and full blood count (FBC) should be monitored at baseline and after 4 to 6 weeks of treatment for courses lasting longer than 4 weeks.[6] Serious adverse reactions usually occur within 1 to 2 months of starting oral terbinafine.[4,5] and will often resolve within a week of ceasing therapy.[5] However some reactions, including loss or alteration of taste can be prolonged.[2]

In New Zealand, some adverse reactions have resulted in admission to hospital, and some of these episodes such as blood dyscrasias, have been life-threatening.[4,6] There have also been deaths attributable to terbinafine therapy. [3,4]

ADVISE PATIENTS TO REPORT SYMPTOMS OF HEPATOTOXICITY AND ANY SKIN REACTIONS

Health professionals should always advise patients taking terbinafine to be alert for the symptoms of infection or neutropenia (eg fever, sore throat, mouth ulcers),[4,5] symptoms suggestive of liver impairment (eg abdominal pain, jaundice, persistent nausea),[2,6,10] and any other reaction associated with terbinafine including progressive skin rash, taste perversion or loss, or hair loss.[1,2]

Patients, especially those who have been taking terbinafine for more than one month, should report these symptoms promptly so that clinical investigations including blood tests can be arranged urgently and terbinafine therapy stopped immediately.[2] A delay in diagnosis is likely to be associated with an increase in morbidity and mortality.[4,5]

ALWAYS CONFIRM PRESENCE OF SUSCEPTIBLE FUNGAL ORGANISMS BEFORE PRESCRIBING

Terbinafine should only be used when there is a clear indication for its use, and when terbinafine therapy is clinically appropriate.[5,6,7] Empirical therapy should be avoided. Complications of nail infections are uncommon but may occur in patients who have diabetes, underlying vascular disease of connective tissue disorders.[7]

To maximise the safety and efficacy of oral terbinafine ensure that the infection is caused by a susceptible fungal organism before prescribing this medicine.[6,7] Nail clippings or skin scrapings should be sent for microscopic examination and culture. Microscopy results become available within 3 to 5 days. Samples will be incubated for up to 4 weeks before being reported as culture negative.[7] Laboratory diagnosis is recommended before starting treatment because other conditions can present similarly, particularly psoriasis. When mycology was performed on patients referred to a dermatologist for treatment of onychomycosis, 54 % did not have a fungal infection.[5]

Other non-fungal conditions which may present with similar symptoms include trauma, lichen planus, and vascular disorders.[6,7]

CONSIDER THE BENEFITS OF TERBINAFINE AGAINST POTENTIAL FOR HARM

The benefits of using oral terbinafine to treat relatively common fungal infections of the skin or nails (many of

➥ continued

which may be trivial and asymptomatic) should be weighed against the risk of harm to the patient.[5,6]

The implications of using terbinafine should be discussed with the patient, in particular, the long duration of treatment (up to several months), the potential side-effects of treatment, and that there is no guarantee that terbinafine use will result in a cure.[7,8] A review of data from 8 studies showed that standard courses of terbinafine achieved a disease-free nail (clinically normal nail with negative results on microscopy and culture) in 44% of patients.[9] Patients should always be informed that the nail may not look completely normal, even after treatment.[6] Treatment may not be necessary for everybody and may be inappropriate for elderly people or people taking multiple medicines as there is an increased risk of adverse effects and drug interactions.[6]

Many patients may elect not to use oral terbinafine when informed of the potential side-effects and low cure rate.

If initial treatment fails; confirm mycology and check adherence to treatment. An alternative medicine may be more appropriate.[7]

The usual adult dose of terbinafine is 250 mg daily. Duration of treatment depends on the site and extent of the infection. It is well absorbed orally with and without food and is concentrated in the skin and nails. It may persist in the skin and nails, long after the drug is stopped.

Patients with renal impairment (creatinine clearance less than 50 mL/min) should receive half the normal dose. Treatment should be avoided for patients with creatinine clearance less than 20 mL/min because there is no information on its use in these patients.

Terbinafine is not recommended for patients with chronic or active liver disease, psoriasis or systemic lupus erythematosus (SLE) because these conditions can be exacerbated.[1,2,9]

Terbinafine is a moderate inhibitor of cytochrome p450 2D6 enzymes and may interfere with the metabolism of many other medications via this pathway which include flecainide, beta blockers, MAOIs, SSRIs and TCAs. The metabolism of terbinafine itself may be increased or decreased by a number of cytochrome p450 enzyme interactions with other medicines including rifampicin, cimetidine, and fluconazole.

Prescribers should be aware of clinically relevant medicine interactions before prescribing. These are listed in the data sheet and The New Zealand Formulary.[1,2]

Pregnancy and breastfeeding.

There is no human data for the use of terbinafine in pregnancy, so it is advisable to wait to begin treatment until after pregnancy.[1,13] Terbinafine should not be administered to breastfeeding mothers as it is excreted into breast milk.[2,13]

REFERENCES

1. New Zealand Formulary Terbinafine http://www.nzf.org.nz/nzf_3341.html?searchterm=terbinafine (Accessed 12-10-18)
2. Rex Medical Limited. Terbinafine tablets data sheet 11-09-17. http://www.medsafe.govt.nz/profs/Datasheet/d/deolatetab.pdf (accessed 12-10-18)
3. Medsafe, Wellington. Medicines Adverse Reactions Committee 127th Meeting Minutes 14 September 2006; Oral Terbinafine Serious Adverse Reactions. http://www.medsafe.govt.nz/Profs/adverse/Minutes127.htm#2.1.12 (accessed on 12-10-18)
4. Pillans P, Boyd I. Toenails and agranulocytosis. Intern Med J 2007 Aug;37(8)572-575 (Accessed 12-10-18)
5. Medsafe Pharmacovigilance Team. Terbinafine: serious hepatic and haematological reactions. Prescriber Update 2006;27(2):18-20 http://www.medsafe.govt.nz/Profs/PUarticles/watchingbriefsNov06.htm#Terbinafine (Accessed 23-10-18)
6. bpac 2009, Management of fungal nail infections. http://www.bpac.org.nz/BPJ/2009/february/docs/bpj19_fungalnail_pages_18-23.pdf (Accessed 23-10-18)
7. How should fungal nail infection be treated? Drug Ther Bull 2008;46(1):3-8
8. Epstein E. How often does oral treatment of toenail onychomycosis produce a disease-free nail? Arch Dermatol 1998;134(12):1551-4 (Accessed 23-10-18)
9. Kalinska-Bienias A, Kowalewski C, Wozniak K. Terbinafine-induced subacute cutaneous lupus erythematosus in two patients with systemic lupus erythematosus successfully treated with topical corticosteroids. Postepy Dermatologii I Alergologii 2013;4:261-4
10. bpac 2014 Tinea pedis:not just the curse of the athlete https://bpac.org.nz/BPJ/2014/December/tinea-pedis.aspx (Accessed 23-10-18)
11. Medsafe, Wellington. MARC 136th meeting Minutes 11-12-2008 http://www.medsafe.govt.nz/profs/adverse/Minutes136.htm (Accessed 23-10-18)
12. Oakley A, What is terbinafine? Dermnet NZ https://www.dermnetnz.org/topics/terbinafine (Accessed 23-10-18)
13. Pilmis B, Vincent J, Sobel J, Lecuit M, Lortholary and Charlier C, Antifungal drugs during pregnancy: an updated review (Journal of Antimicrobial Chemotherapy, Volume 70, Issue 1, January 2015, Pages 14–22 accessed 28-10-18)

ACKNOWLEDGEMENTS

We wish to thank Dr Kerry Read, Infectious Diseases Consultant and Kristen Bondesio, Antimicrobial Stewardship Pharmacist at Waitematā District Health Board, for their valuable contribution

No: 00182-01-027, Issued March 2019; Review: March 2022