SAFER®
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, and ringworm infections 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, 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 reactions associated with oral terbinafine are gastrointestinal including abdominal discomfort, anorexia, nausea and diarrhoea. Rash and urticaria can also occur, sometimes associated with arthralgia or myalgia.[1] Taste disturbance or loss is one of the most common reactions associated with terbinafine that is reported to CARM (Centre for Adverse Reactions Monitoring) in New Zealand.[3]

The CARM database also contains reports of more serious adverse reactions that have been linked to terbinafine use. Hepatotoxicity (eg cholestatic jaundice) and dermatological reactions (eg Stevens-Johnson syndrome) feature prominently, and are sometimes serious.[2,4] There is a causal link between oral terbinafine and serious blood dyscrasias, including agranulocytosis and severe neutropenia.[2,5] Due to the rarity of these adverse reactions, routine haematological monitoring is not indicated,[5] however, baseline LFT (liver function tests) and FBC (full blood count) may be appropriate for some patients. Ongoing monitoring may also be indicated, particularly for patients taking other medicines with hepatotoxic or myelosuppressive potential.

Serious adverse reactions usually occur within 1 - 2 months of starting oral terbinafine,[5,6] and will often resolve within a week of ceasing therapy.[5] Some reactions, including loss or alteration of taste can be prolonged,[2] and in some cases last for several years.

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.[6] Although no fatalities have been reported in New Zealand,[6] deaths attributable to terbinafine therapy have been reported elsewhere.[3]

ADVISE PATIENTS TO REPORT SYMPTOMS OF HEPATOTOXICITY AND ANY SKIN REACTIONS

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

Patients should be advised to report these symptoms promptly so that clinical investigations 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.[5]

ALWAYS CONFIRM PRESENCE OF SUSCEPTIBLE FUNGAL ORGANISMS BEFORE PRESCRIBING

Terbinafine should only be used when prescribers are confident that there is a clear indication for its use, and that terbinafine therapy is clinically appropriate;[6] empirical therapy should be avoided.

To maximise the safety and efficacy of oral terbinafine, ensure that the infection is caused by a susceptible fungal organism before prescribing.[6] Nail clippings or skin scrapings should be sent for microscopic examination and culture. Microscopy results usually become available within 3-5 days. Samples can 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. Non-fungal conditions which may present with similar symptoms include trauma, lichen planus, and vascular disorders.[6,7] When mycology was performed on patients referred to a dermatologist for treatment of onychomycosis, 54% did not have a fungal infection.[6]

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TERBINAFINE

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

The implications of using terbinafine should be discussed with the patient, in particular: the long duration of treatment (up to several months),[7] the potential side-effects of treatment, and that there is no guarantee that terbinafine use will result in a cure.[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. 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 interactions.[7]

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

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

The usual adult dose of terbinafine is 250mg daily; the duration of treatment depends on the site and extent of the infection. Patients with renal impairment (creatinine clearance less than 50mL/min) should receive half the normal dose. Terbinafine should be avoided if the creatinine clearance less than 20mL/min.

Terbinafine is not recommended for patients with chronic or active liver disease, psoriasis[2] or systemic lupus erythematosus (SLE)[10] because these conditions can be exacerbated.[1]

Prescribers should be aware of a number of clinically relevant interactions with other medicines before prescribing. These are listed in the data sheet[2] and The New Zealand Formulary.[1]

Terbinafine is pregnancy category B1, so due to the lack of information available in pregnant women, it is best avoided unless the potential benefit outweighs the risk. Terbinafine should be avoided if breastfeeding, again due to the lack of data.[1]

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REFERENCES

1. New Zealand Formulary Terbinafine www.nzf.org.nz/nzf_3341.html?searchterm=terbinafine (Accessed 07-03-14)
2. Douglas Pharmaceuticals Limited. Terbinafine-DP tablets data sheet 10-12-12. www.medsafe.govt.nz/profs/datasheet/t/Terbinafine-DPtab.pdf (Accessed 07-03-14)
3. Joint Adverse Event Notifications System (JAENS). www.anztpa.org (Accessed 07-13-14)
4. Medsafe, Wellington. Medicines Adverse Reactions Committee 127th Meeting Minutes 14 September 2006; Oral Terbinafine Serious Adverse Reactions. www.medsafe.govt.nz/Profs/adverse/Minutes127.htm#2.1.12 (accessed on 22 Jan 09)
5. Pillans P, Boyd I. Toenails and agranulocytosis. Int Med Jnl 2007;37:572-575
6. Medsafe Pharmacovigilance Team. Terbinafine: serious hepatic and haematological reactions. Prescriber Update 2006;27(2):18-20. www.medsafe.govt.nz/Profs/PUarticles/watchingbriefsNov06.htm#Terbinafine (Accessed 07-03-14)
7. Management of fungal nail infections. Best Practice Journal 2009;19:18-23 www.bpac.org.nz/BPJ/2009/february/docs/bpj19_fungalnail_pages_18-23.pdf (Accessed 07-03-14)
8. How should fungal nail infection be treated? Drug Ther Bull 2008;46(1):3-8
9. Epstein E. How often does oral treatment of toenail onychomycosis produce a disease-free nail? Arch Dermatol 1998;134(12):1551-4
10. 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

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