SAFER®
SAFER USE OF HIGH RISK MEDICINES

Waitemata District Health Board
Te Wai Awhina

TERBINAFINE - SAFE PRESCRIBING - NAIL IT!

- CAN CAUSE SERIOUS ADVERSE REACTIONS
- REACTIONS ARE MOSTLY HEPATIC AND SKIN DISORDERS; BLOOD DYSCRASIAS OCCUR RARELY
- CURRENTLY NO FATALITIES FROM TERBINAFINE IN NZ, BUT HAS LED TO HOSPITALISATIONS
- ALWAYS ADVISE PATIENTS TO REPORT SYMPTOMS OF ADVERSE REACTIONS
- ALWAYS CONFIRM PRESENCE OF SUSCEPTIBLE FUNGAL ORGANISMS
- CONSIDER BENEFITS OF TERBINAFINE AGAINST POTENTIAL FOR HARM

TERBINAFINE CAN CAUSE SERIOUS ADVERSE REACTIONS

Oral terbinafine use is associated with a number of rare, but potentially serious adverse reactions[1]. It is because of this potential toxicity that we consider terbinafine to be a 'high-risk' medicine.

ADVERSE REACTIONS ARE MOSTLY HEPATIC AND SKIN DISORDERS; BLOOD DYSCRASIAS CAN OCCUR RARELY

The Centre for Adverse Reactions Monitoring (CARM) database contains New Zealand reports of adverse reactions that have been linked to terbinafine use[2]; many of these have also been reported elsewhere in the medical literature[3,4]. These reactions are suggestive of a drug hypersensitivity syndrome[5].

Hepatotoxicity (e.g. cholestatic jaundice) and dermatological reactions (e.g. Stevens-Johnson syndrome) feature prominently, and are sometimes serious[1,2]. There is also a causal link between oral terbinafine use and serious blood dyscrasias, including agranulocytosis and severe neutropenia[1,4]. Despite this, routine haematological monitoring is not indicated for patients on terbinafine therapy[4].

Most adverse reactions occur within two months of starting terbinafine[6], although a case series of neutropenic episodes associated with terbinafine use reported these reactions after only four weeks of therapy[4]. Adverse reactions with terbinafine will often resolve within a week of ceasing therapy[7]; however loss of (or altered) taste has been reported to persist for many months[1]. None of these serious reactions have been reported with topical terbinafine therapy[8].

CURRENTLY NO FATALITIES FROM TERBINAFINE USE REPORTED IN NZ, BUT ITS USE HAS LED TO HOSPITALISATIONS

In New Zealand, some adverse reactions have resulted in admission to hospital (CARM report nine admissions by 2006), and some of these episodes have been life-threatening (blood dyscrasias)[6]. Although no fatalities have been reported in New Zealand[6], deaths attributable to terbinafine therapy have been reported elsewhere (due to hepatic, skin and haematological toxicities)[2].

ALWAYS ADVISE PATIENTS TO REPORT SYMPTOMS OF ADVERSE REACTIONS

Health professionals should always advise patients taking terbinafine to be alert for the symptoms of infection or neutropenia (e.g. fever, sore throat, mouth ulcers), symptoms suggestive of liver impairment (e.g. abdominal pain, jaundice)[1], and any other potential reaction (e.g. taste perversion or loss[9], severe skin reactions[1], or hair loss).

Patients, especially those who have been taking terbinafine for more than one month[7], should report these symptoms promptly so that clinical investigations (e.g. blood tests) can be commenced immediately and terbinafine therapy stopped[1]; a delay in diagnosis is likely to be associated with an increase in morbidity and mortality[8].

ALWAYS CONFIRM THE PRESENCE OF SUSCEPTIBLE FUNGAL ORGANISMS

Terbinafine should only be used when prescribers are confident that there is a clear indication for its use, and terbinafine therapy is clinically appropriate[6]; empirical therapy should be avoided[10].

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TERBINAFINE

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]. Diagnosis is usually confirmed mycologically, although this may require multiple samples at intervals of many months[11].

It should also be remembered that some non-fungal causes may have symptoms that are similar to fungal nails, including: trauma, psoriasis, lichen planus, and vascular disorders[6,11]. An unpublished New Zealand study found that when mycology was performed on patients referred to a dermatologist for treatment of onychomycosis, 54% did not have a fungal infection[6].

CONSIDER THE BENEFITS OF TERBINAFINE AGAINST THE 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, the potential side-effects of treatment, and that there is no guarantee that terbinafine use will result in a cure[11]. A review of data from seven studies showed that only 44% of patients treated with terbinafine had clinically normal nails with negative results on microscopy and culture one year later[12]. Complications from fungal nail infection are also uncommon[11].

All of these factors will influence a patient's decision about embarking on terbinafine therapy[11]; an anecdotal report from a Waitemata DHB general practitioner stated that many patients elect not to use oral terbinafine when informed of the potential side-effects and low cure rate[13].

Prescribers are reminded that the shortest possible course of terbinafine should be used[14]. Terbinafine is not recommended for patients with chronic or active liver disease, or psoriasis[1]. Patients with renal impairment require dose modification, and doctors should be aware of a number of clinically relevant medicine interactions[1].

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