

Hearing Impairment Associated with Oral Terbinafine Use; A Case Series and Case/Non-Case Analysis in the Netherlands Pharmacovigilance Centre Lareb Database and VigiBase

Joep H.G. Scholl and Eugene P. van Puijenbroek Netherlands Pharmacovigilance Centre Lareb, 's-Hertogenbosch, the Netherlands

Abstract

Background: The Netherlands Pharmacovigilance Centre Lareb received reports of six cases of hearing impairment in association with oral terbinafine use. This study describes these cases and provides support for this association from the Lareb database for spontaneous adverse drug reaction (ADR) reporting and from Vigibase, the ADR database of the WHO Collaborating Centre for International Drug Monitoring, the Uppsala Monitoring Centre.

Objectives: The objective of the current study was to identify whether the observed association between oral terbinafine use and hearing impairment, based on cases received by Lareb, constitutes a safety signal.

Methods: Cases of hearing impairment in oral terbinafine users are described. In a case/non-case analysis, the strength of the association in Vigibase and the Lareb database was determined (date of analysis August 2011) by calculating the reporting odds ratios (RORs), adjusted for possible confounding by age, sex and ototoxic concomitant medication. For the purpose of this study, RORs were calculated for deafness, hypoacusis and the combination of both, defined as hearing impairment.

Results: In the Lareb database, six reports concerning individuals aged 31–82 years, who developed hearing impairment after starting oral terbinafine, were present. The use of oral terbinafine was disproportionally associated with hypoacusis in both the Lareb database (adjusted ROR 3.9; 95% CI 1.7, 9.0) and in Vigibase (adjusted ROR 1.7; 95% CI 1.0, 2.8). Deafness was not disproportionally present in either of the databases.

Discussion: Based on the described cases and the statistical analyses from both databases, a causal relationship between the use of oral terbinafine and hearing impairment is possible. The mechanism by which terbinafine could cause hearing impairment has not been elucidated yet. The pharmacological action of terbinafine is based on the inhibition of squalene epoxidase, an enzyme present in both fungal and human cells. This inhibition might result in a decrease in cholesterol levels in human cells, among which are the outer hair cells of the cochlea. It may be possible that the reduction in cochlear

For more information, please contact info@lareb.nl