NIZORAL (KETOCONAZOLE): POTENTIAL FOR FATAL LIVER INJURY, SIGNIFICANT DRUG INTERACTIONS AND ADRENAL GLAND PROBLEMS

This special issue is prompted by notification that the FDA is intending to limit ketoconazole use, adding new drug warnings, as well as a new medication guide. The verbatim safety alert from the FDA is posted below for review. Please call SUGDIS at 205-726-2659 with any further questions.

ISSUE: FDA is taking several actions related to Nizoral (ketoconazole) oral tablets, including limiting the drug’s use, warning that it can cause severe liver injuries and adrenal gland problems, and advising that it can lead to harmful drug interactions with other medications. FDA has approved label changes and added a new Medication Guide to address these safety issues. As a result, Nizoral oral tablets should not be a first-line treatment for any fungal infection. Nizoral should be used for the treatment of certain fungal infections, known as endemic mycoses, only when alternative antifungal therapies are not available or tolerated.

Liver Injury (Hepatotoxicity)
Nizoral tablets can cause liver injury, which may potentially result in liver transplantation or death. FDA has revised the Boxed Warning, added a strong recommendation against its use (contraindication) in patients with liver disease, and included new recommendations for assessing and monitoring patients for liver toxicity.

Adrenal Insufficiency
Nizoral tablets may cause adrenal insufficiency by decreasing the body’s production of corticosteroids.

Drug Interactions
Nizoral tablets may interact with other drugs a patient is taking and can result in serious and potentially life-threatening outcomes, such as heart rhythm problems. See the FDA Drug Safety Communication for additional information, including a Data Summary.

BACKGROUND: Nizoral (ketoconazole) is indicated for the treatment of fungal infections when alternatives are not available or not tolerated. The topical formulations of Nizoral have not been associated with liver damage, adrenal problems, or drug interactions. These formulations include creams, shampoos, foams, and gels applied to the skin, unlike the Nizoral tablets, which are taken by mouth.

RECOMMENDATION: Nizoral tablets should be used only for the treatment of certain life-threatening mycoses when the potential benefits outweigh the risks and alternative therapeutic options are not available or tolerated. Healthcare professionals should assess the liver status of the patient before starting oral ketoconazole, and monitor serum ALT levels during treatment. Adrenal function should be monitored in patients with adrenal insufficiency or with borderline adrenal function and in patients under prolonged periods of stress (major surgery, intensive care, etc.). Review all concomitant medications for the potential for drug interactions with Nizoral tablets.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: [www.fda.gov/MedWatch/report.htm](http://www.fda.gov/MedWatch/report.htm)
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178


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