U.S. Food and Drug Administration
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Drug Safety Communications

FDA Drug Safety Communication

FDA warns that prescribing of Nizoral (ketoconazole) oral tablets for unapproved uses including skin and nail infections continues; linked to patient death

This is an update to the FDA Drug Safety Communication: FDA limits usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems issued on July 26, 2013.

Safety Announcement

[05-19-2016] The U.S. Food and Drug Administration (FDA) is warning health care professionals to avoid prescribing the antifungal medicine ketoconazole oral tablets to treat skin and nail fungal infections. Use of this medication carries the risk of serious liver damage, adrenal gland problems, and harmful interactions with other medicines that outweigh its benefit in treating these conditions, which are not approved uses of the drug.

We approved label changes for oral ketoconazole tablets in 2013 to reflect these serious risks and to remove the indication for treatment of skin and nail fungal infections. However, an FDA safety review found that oral ketoconazole continues to be prescribed for these types of conditions. In the 18 months ending in June 2015, skin and nail fungal infections were the only diagnoses[1] cited for the use of oral ketoconazole in an office-based physician surveys database.[2] Since the 2013 labeling changes, one patient death has been reported to the FDA due to liver failure associated with oral ketoconazole prescribed to treat a fungal infection of the nails.

Health care professionals should use ketoconazole tablets only to treat serious fungal infections when no other antifungal therapies are available. Skin and nail fungal infections in otherwise healthy persons are not life-threatening, and so the risks associated with oral ketoconazole outweigh the benefits. Other treatment options are available over-the-counter and by prescription, but are also associated with risks that should be weighed against their benefits.

Patients should discuss with their health care professionals the risks and benefits of available therapies before using any medicine to treat skin and nail fungal infections. Patients taking ketoconazole tablets should seek medical attention right away if they experience any of these signs and symptoms of liver problems, which include loss of appetite, nausea, vomiting, or abdominal discomfort; yellowing of the skin or the whites of the eyes (jaundice); unusual darkening of the urine or lightening of the stools; or pain and discomfort in the right upper abdomen where the liver is located.

Ketoconazole in tablet form is indicated to treat serious infections caused by fungi and should be used only when other effective therapy is not available or tolerated. It works by killing the

fungus or preventing it from growing. During the 12-month period ending in June 2015, approximately 217,000 patients received dispensed prescriptions for oral ketoconazole from U.S. outpatient retail pharmacies.[3] Ketoconazole is only available as a generic. The topical forms of ketoconazole that are applied to the skin or nails have not been associated with liver damage, adrenal problems, or drug interactions.

In a July 2013 Drug Safety Communication, we warned that ketoconazole tablets should not be used as a first-line treatment for any fungal infection because it can cause severe liver injury and adrenal gland problems, and advised it can lead to harmful interactions with other medicines. We determined that the risks outweigh the benefits for treating skin and nail fungal infections and approved label changes removing this indication from the drug label and limited its labeled indication to treating only serious fungal infections.

We urge health care professionals and patients to report side effects involving ketoconazole to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

References

1. Diagnoses captured for ICD-9 codes 111.x,110.s, and 782.x.
2. Encuity Research, LLC, Treatment Answers (TM). Jan 2012 through June 2014 & Jan 2014 through June 2015. Extracted August 2015.
3. IMS Health: Vector One® Total Patient Tracker (TPT). July 2014-June 2015. Extracted August 2015.

Related Information

The FDA's Drug Review Process: Ensuring Drugs are Safe and Effective
http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143534.htm

Thinking it Through: Managing the Benefits and Risks of Medicines
http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143558.htm