BlueCross BlueShield Federal Employee Program

KETOCONAZOLE TABLETS

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Ketoconazole is an imidazole antifungal agent available as an oral tablet and various topical formulations. Ketoconazole works by weakening the structure and function of the fungal cell membrane. Due to potential for severe adverse events, ketoconazole tablets should only be used when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweigh the potential risks. For the management of prostate cancer, ketoconazole tablets inhibit androgen (1-2).

Regulatory Status

FDA-approved indications: Ketoconazole oral is indicated for the treatment of the following systemic fungal infections in patients who have failed or who are intolerant to other therapies: *blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis*, and *paracoccidioidomycosis*. Ketoconazole should not be used for fungal meningitis because it penetrates poorly into the cerebrospinal fluid. Ketoconazole tablets are not indicated for the treatment of fungal infections of the skin or nails (1-2).

Off-Label Use:

Ketoconazole is an imidazole antifungal agent that inhibits adrenal androgen synthesis. Ketoconazole is a standard secondary hormonal therapy for patients with castration-resistant prostate cancer. The published dose of ketoconazole for metastatic castrate resistant prostate cancer is 200 to 400 mg three times a day (3).

Ketoconazole has a boxed warning regarding serious hepatotoxicity, QT prolongation, and drug interactions leading to QT prolongation (1).

Serious hepatotoxicity, including cases with a fatal outcome or requiring liver transplantation has occurred with the use of oral ketoconazole. Ketoconazole tablets is contraindicated in patients with acute or chronic liver disease. Patients receiving oral ketoconazole should be informed by the prescriber of the risk and should be closely monitored. At baseline, obtain laboratory tests (e.g., serum gamma-glutamyl transferase (SGGT), alkaline phosphatase, ALT, AST, total bilirubin (TBL), prothrombin time (PT), international normalization ratio (INR), and testing for viral hepatitides). During the course of treatment, serum ALT should be monitored weekly for

the duration of treatment. If ALT values increase to a level above the upper limit of normal or 30 percent above baseline, or if the patient develops symptoms, ketoconazole treatment should be interrupted, and a full set of liver tests should be obtained (1).

Ketoconazole tablets can prolong the QT interval. Co-administration of the following drugs with ketoconazole is contraindicated: dofetilide, quinidine, pimozide, cisapride, methadone, disopyramide, dronedarone and ranolazine. Ketoconazole can cause elevated plasma concentrations of these drugs which may prolong the QT interval, sometimes resulting in life-threatening ventricular dysrhythmias such as torsades de pointes (1).

Ketoconazole tablets have warnings for enhanced sedation, myopathy, ergotism, liver disease, hypersensitivity, adrenal insufficiency, adverse reactions associated with unapproved uses and hypersensitivity (1).

The safety and effectiveness of Ketoconazole in pediatric patients less than 2 years of age have not been established (1).

Summary

Ketoconazole is an imidazole antifungal agent available as an oral tablet and various topical formulations. Ketoconazole tablets should only be used when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweigh the potential risks. For the management of prostate cancer, ketoconazole tablets inhibit androgen. Ketoconazole tablets carry a boxed warning for hepatotoxicity, QT prolongation and drug interactions leading to QT prolongation. Ketoconazole tablets is contraindicated in patients with acute or chronic liver disease. Ketoconazole tablets have warnings for enhanced sedation, myopathy, ergotism, liver disease, hypersensitivity, adrenal insufficiency, adverse reactions associated with unapproved uses and hypersensitivity. The safety and effectiveness of Ketoconazole in pediatric patients less than 2 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of ketoconazole tablets while maintaining optimal therapeutic outcomes.

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References

1. Ketoconazole [package insert]. Morgantown, WV: Mylan Pharmaceuticals, Inc.; March 2018.
2. Ketoconazole. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; publication year 2021. Available from: http://www.clinicalkey.com.
3. NCCN Drugs & Biologics Compendium® Ketoconazole 2024. National Comprehensive Cancer Network, Inc. Accessed on April 18, 2024.