

 	<i>KETOCONAZOLE</i>
<i>Common Technical Document Module 2.7</i>	Clinical Summary Updated, September 2024
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All redactions  
under Section 41  
and Section 43 of  
the Freedom of  
Information Act.

## **KETOCONAZOLE**

**shampoo 2%**

### **2.7.2 Summary of clinical pharmacology studies**

<div style="background-color: black; width: 100%; height: 15px; margin-bottom: 5px;"></div> <div style="background-color: black; width: 100%; height: 15px;"></div>	<b>KETOCONAZOLE</b>
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## **2.7.2 Summary of clinical pharmacology studies**

### **2.7.2.1 Pharmacodynamic properties**

Ketoconazole is an imidazole-dioxolane antimycotic, active against yeasts, including *Malassezia* and dermatophytes (Van Tyle, et al 1984; Buxton, 1988; Sohn, 1982). Its broad spectrum of activity is already well known. (Van Tyle, et al 1984; Borgers, et al. 1983; Nagpal, et al. 2003; Kyle and Dahl, 2004).

Ketoconazole works as an antifungal agent by inhibiting the cytochrome P450 14 $\alpha$ -demethylase enzyme (Rajendiran, et al., 2021). This enzyme is responsible for inhibiting the biosynthesis of triglycerides and phospholipids by fungi (Van Tyle, et al 1984). More specifically, ketoconazole inhibits the synthesis of lanosterol, a necessary precursor for ergosterol biosynthesis. Ergosterol is needed to maintain the integrity of the membrane of fungi. Without ergosterol, the fluidity of the membrane increase, which in turn prevents fungal growth (Smith and Henry, 1984; Van Tyle, et al 1984; Borgers, et al. 1983; Van den Bossche, 1980). Ketoconazole inhibits the activity of the enzyme 21-hydroxylase. This enzyme is essential for synthesizing mineralocorticoids and glucocorticoids, such as cortisol, in the adrenal cortex. By inhibiting enzymes involved in cortisol synthesis, ketoconazole can be a treatment option for Cushing syndrome (Sinawe and Casadesus, 2022).

#### ***Spectrum of Activity***

Ketoconazole is active against yeasts, including *Malassezia* and dermatophytes. (Van Tyle, et al 1984; Buxton, 1988; Sohn, 1982). Its broad spectrum of activity is already well known. The antifungal properties of ketoconazole were investigated both in vitro and in vivo (Odds, et al 1980; Van Cutsem 1983; Van den Bossche, et al. 1980, Graybill, et al. 1980; Fernández-Torres, et al 2000).

### **2.7.2.2 Pharmacokinetic properties**

Plasma concentrations of ketoconazole were not detectable after topical administration of ketoconazole 2% shampoo on the scalp (Chowdhry and Gupta, 2016).

Plasma levels were detected after topical administration of ketoconazole 2% shampoo on the whole body (Mitu MA et al 2011).