	<i>KETOCONAZOLE</i>
<i>Common Technical Document Module 2.6</i>	Non-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%

2.6.3 Pharmacology tabulated summary

Pharmacology tabulated summary

Table 1. In Vitro Activity of Ketoconazole

Organism	MIC (µg/ml)
<i>Aspergillus sp.</i>	1.00-100
<i>Blastomyces dermatitidis</i>	0.005-2.0
<i>Candida sp</i>	0.02-80
<i>Cryptococcus neoformans</i>	0.10-32
<i>Coccidioides immitis</i>	0.050-1.8
<i>Histoplasma capsulatum</i>	0.10-0.5
<i>Paracoccidioides brasiliensis</i>	0.002-0.008

(Van Tyle et al 1984)

Table 2 Minimal Inhibitory concentrations of ketoconazole for opportunistic yeast pathogens: tests performed in Saborayd’s broth at 37° C

Species tested	Number tested	Number sensitive to ketoconazole at (mg/l):										
		0.1	0.2	0.4	0.8	1.6	3.1	6.3	12.5	25	50	> 50
<i>C. albicans</i>	37	1	1	1	3			2	7	8	14	
<i>C. guilliermondii</i>	4			2						1	1	
<i>C. krusei</i>	8		1	1	1	1	4					
<i>C. parapsilosis</i>	5		2		1					1	1	
<i>C. pseudotropicalis</i>	2									1		1
<i>C. stellatoidea</i>	1				1							
<i>C. tropicalis</i>	6			1		1	1			2	1	
<i>T. glabrata</i>	14				1	1		1	5	3	3	
Totals	77	1	4	5	7	3	5	3	12	16	20	1

(Odds, et al 1980)

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Table 3 Minimum Inhibitory Concentration of ketoconazole against a variety of yeasts and fungi

Organism	No. of Strains Tested	Range of Minimal Inhibitory Conc. (mcg/mL)
Dermatophytes		
Microsporum canis	24	0.1 – 64
Microsporum audouini	4	2 – 64
Microsporum gypseum	9	0.1 – 64
Microsporum cookie	1	1
Trichophyton mentagrophytes	24	0.1 – 20
Trichophyton rubrum	75	10 ⁻³ – 128
Trichophyton labelloid	1	1
Trichophyton schoenleini	1	1
Trichophyton tonsurans	35	0.25 – 16
Epidermophyton floccosum	23	0.1 -8
Trichophyton verrucosum	8	0.1 -1
Trichophyton violaceum	3	1
Yeasts		
Candida albicans	472	0.02–80
Candida tropicalis	45	0.1–80
Candida pseudotropicalis	2	25–50
Candida guilliermondii	4	0.4–50
Candida krusei	14	0.2–31
Candida parapsilosis	18	0.2–64
Candida stellatoidea	1	0.8
Cryptococcus neoformans	39	0.1–32
Torulopsis glabrata	124	0.8–64
Rhodotorula mucilaginosa	1	0.1
Trichosporon cutaneum	1	0.1
Dimorphic Fungi		
Blastomyces dermatitidis	26	0.1–2
Coccidioides immitis	30	0.1–0.8
Histoplasma capsulatum	26	0.1–0.5
Paracoccidioides brasiliensis	5	0.002–0.1
Eumycetes		
Acremonium falciforme	1	10
Madurella grisea	1	0.1
Madurella mycetomi	1	0.1
Petriellidium boydii	23	0.1–4
Actinomycetales		
Actinomadura madurae	2	10–25
Nocardia asteroides	1	1
Nocardia brasiliensis	2	10–32
Nocardia cavea	1	1
Streptomyces sp.	1	10

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(continued)

Organism	No. of Strains Tested	Range of Minimal Inhibitory Conc. (mcg/mL)
Phycomycetes		
<i>Absidia corymbifera</i>	1	1
<i>Rhizopus nigricans</i>	1	100
<i>Saprolegnia</i> sp.	1	1
Various Fungi		
<i>Aspergillus flavus</i>	2	1
<i>Aspergillus fumigatus</i>	55	1-100
<i>Aspergillus glaucus</i>	1	1
<i>Aspergillus nidulans</i>	1	1
<i>Aspergillus niger</i>	6	1-16
<i>Aspergillus terreus</i>	3	1
<i>Aspergillus</i> sp.	3	5.5-100
<i>Geotrichum candidum</i>	1	1
<i>Piedraia hortai</i>	1	0.1
<i>Sporothrix schenckii</i>	23	0.1-16
Dematiaceous Fungi^a	29	0.1-64

^a *Cladosporium* sp., *Fonsecaea* sp. and *Phialophora* sp.

(Product Monograph_Ketoconazole)

Table 4
Minimal Inhibitory concentrations of ketoconazole and miconazole for opportunistic yeast pathogens: tests performed in Rowleys-Huber broth at 30° C

Species tested	No. tested	Antifungal	Number sensitive to (mg/l):									
			0.25	0.5	1	2	4	8	16	32	64	> 64
<i>C. albicans</i>	54	ketoconazole						5	6	26	17	
		miconazole					5	16	16	14	3	
<i>C. krusei</i>	2	ketoconazole				2						
		miconazole	2									
<i>C. parapsilosis</i>	7	ketoconazole			2					2	2	1
		miconazole		2	1			1			3	
<i>C. tropicalis</i>	2	ketoconazole					1			1		
		miconazole							1			1
<i>T. glabrata</i>	10	ketoconazole				4	2	1	1	1		1
		miconazole	4		2	1		1	2			
Totals	75	ketoconazole			2	6	3	6	7	30	19	2
		miconazole	6	2	3	1	5	18	19	14	6	1

Table 5 Minimal Inhibitory concentrations of ketoconazole for dermatophytes

Species tested	Number tested	Number sensitive to ketoconazole at (mg/l):						
		1	5	10	15	20	25	50
<i>E. floccosum</i>	3	3						
<i>M. canis</i>	6						2	4
<i>T. mentagrophytes*</i>	4			2	1	1		
<i>T. rubrum</i>	6	1	1	1	3			
Total	19	4	1	3	4	1	2	4

* var. *mentagrophytes*.

(Odds, et al 1980)

Table 6 Assays for Ketoconazole

Type of Assay – Test Conditions	Detection limits (µg/ml)
Bioassay – Organism	
Agar diffusion – <i>Coccidioides immitis</i>	1.0-5
Agar diffusion – <i>Coccidioides immitis</i>	0.123-10
Disk diffusion – <i>Coccidioides immitis</i>	02-20
Agar diffusion – <i>Candida pseudotropicalis</i>	03-50
Chromatographic with extraction	
GLC	0.01-20
HPLC @ 231 nm	0.25-100
HPLC @ 205 nm	0.01-20
HPLC; fluorescence detection @ 206 nm	0.10-20

(Van Tyle et al 1984)

Table 7

Minimal inhibitory concentrations of econazole, ketoconazole and miconazole for *Aspergillus* species

Species tested	Number tested	Antifungal	Number sensitive to (mg/l):							
			0.13	0.25	0.5	1	2	4	8	16
<i>A. flavus</i>	1	ketoconazole				1				
		miconazole				1				
<i>A. fumigatus</i>	25	econazole		1						
		ketoconazole				1	3	4	5	12
		miconazole			2	6	7	5	4	1
<i>A. niger</i>	5	econazole	5	7	4	6	3			
		ketoconazole							2	3
		miconazole				1	3	1		
<i>A. terreus</i>	3	econazole	4	1						
		ketoconazole				3				
		miconazole				3				
Total	34	econazole	2		1					
		ketoconazole				5	3	4	7	15
		miconazole			2	11	10	6	4	1
			11	9	5	6	3			

(Odds, et al 1980)

Table 8

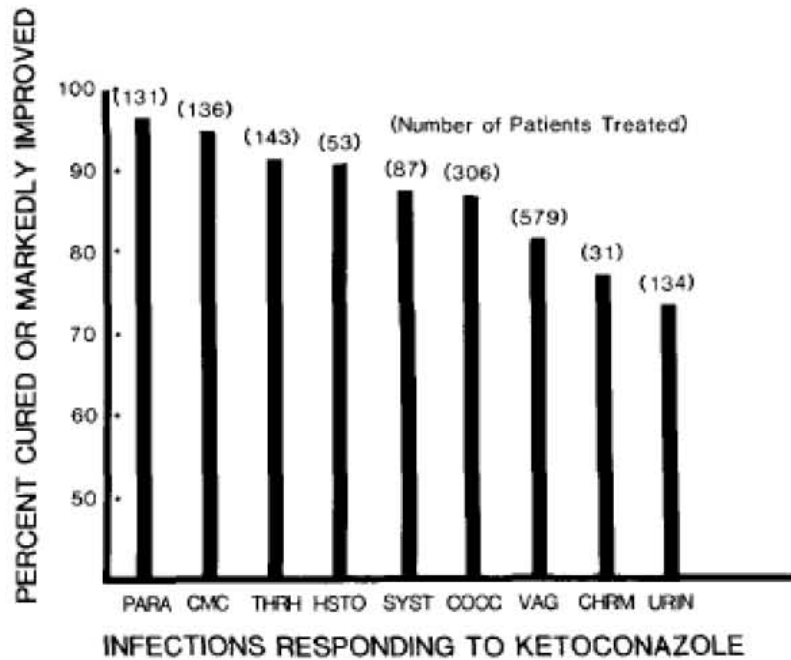
Therapeutic efficacy of ketoconazole in dermatophyte infections in guinea pigs

Animal infected with	No. of treatments	Histological examination‡	
		treated	untreated
<i>T. mentagrophytes</i> *	3	+	++++
	4	+	++++
	5	±	++++
	6	-	++++
<i>M. canis</i> †	3	++	++++
	6	+	++++
	9	-	++++

* Treatment commenced 3 days after infection.
 † Treatment commenced 8 days after infection.
 ‡ Scores ranged from + = a few follicles infected distally, to ++++ = a majority of hair follicles infected at all levels.

(Odds, et al 1980)

Figure 1 Infections responding to Ketoconazole



(Van Tyle et al 1984)