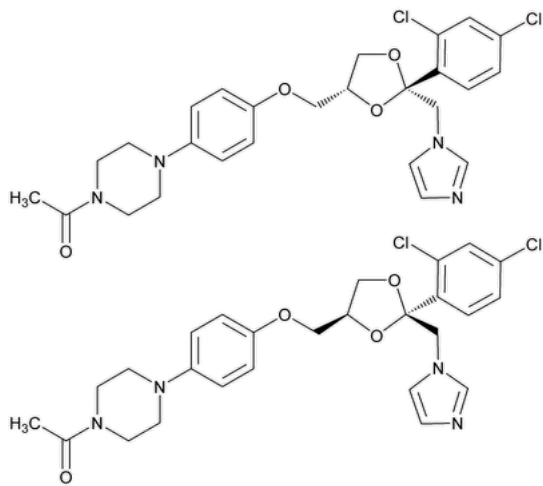


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Ketoconazole



$C_{26}H_{28}Cl_2N_4O_4$ 531.43
Piperazine, 1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-, *cis*-,
(±)-*cis*-1-Acetyl-4-(p-[[2-(2,4-dichlorophenyl)-2-(imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl)piperazine CAS RN®: 65277-42-1; UNII: R9400W927I.

DEFINITION
Ketoconazole contains NLT 98.0% and NMT 102.0% of ketoconazole ($C_{26}H_{28}Cl_2N_4O_4$), calculated on the dried basis.

- IDENTIFICATION**
- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy: 197K*
 - **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

- **PROCEDURE**
Buffer: 3.4 mg/mL of ▲tetrabutylammonium▲ (ERR 1-Oct-2024) hydrogen sulfate in water
Solution A: Acetonitrile and *Buffer* (5:95)
Solution B: Acetonitrile and *Buffer* (50:50)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	0	100
25	0	100
26	100	0
30	100	0

Diluent: Methanol
Standard solution: 0.1 mg/mL of [USP Ketoconazole RS](#) in *Diluent*

Sample solution: 0.1 mg/mL of Ketoconazole in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 10-cm; 3-μm packing L1

Flow rate: 2.0 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ketoconazole ($C_{26}H_{28}Cl_2N_4O_4$) in the portion of Ketoconazole taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Ketoconazole RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ketoconazole in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#)

Sample: 2 g

Acceptance criteria: NMT 0.1%

• **ORGANIC IMPURITIES**

Buffer, Solution A, Solution B, Mobile phase, Diluent, and Chromatographic system: Proceed as directed in the Assay.

Standard solution: 0.01 mg/mL each of [USP Ketoconazole RS](#) and [USP Terconazole RS](#) in *Diluent*

Sample solution 10.0 mg/mL of Ketoconazole in *Diluent*

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between ketoconazole and terconazole peaks

Relative standard deviation: NMT 5.0% for the ketoconazole peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any impurities in the portion of Ketoconazole taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any impurities from the *Sample solution*

r_S = peak response of Ketoconazole from the *Standard solution*

C_S = concentration of [USP Ketoconazole RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ketoconazole in the *Sample solution* (mg/mL)

Acceptance criteria: Disregard any peak less than 0.05%.

Any individual unspecified impurity: NMT 0.10%

Total impurities: NMT 2.0%

SPECIFIC TESTS

• [OPTICAL ROTATION, Specific Rotation \(781S\)](#)

Sample solution: 40 mg/mL in methanol

Acceptance criteria: -1° to $+1^\circ$ at 20°

• [LOSS ON DRYING \(731\)](#)

Analysis: Dry under vacuum at 80° for 4 h.
Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS** (11).

[USP Ketoconazole RS](#)
[USP Terconazole RS](#)

Piperazine, 1-[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-4-(1-methylethyl)-, *cis*-; *cis*-1-(*p*-{[2-(2,4-Dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy}phenyl)-4-isopropylpiperazine.
C₂₆H₃₁Cl₂N₅O₃ 532.46

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
KETOCONAZOLE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

Pharmacopeial Forum: Volume No. PF 40(4)

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