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# Ketoconazole Compounded Oral Suspension

**DEFINITION**
Ketoconazole Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of ketoconazole ($C_{26}H_{28}Cl_2N_4O_4$).

Prepare Ketoconazole Compounded Oral Suspension 20 mg/mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations ⟨795⟩*).

| | |
|---|---|
| Ketoconazole | 2.0 g |
| Cetylpyridinium Chloride | 10 mg |
| Xanthan Gum | 0.15 g |
| Purified Water | 30 mL |
| Suspension Structured Vehicle or Sugar-Free Suspension Structured Vehicle, a sufficient quantity to make | 100 mL |

Place the required number of tablets in a glass mortar, and comminute to a fine powder such that they pass through a 40-mesh or 45-mesh sieve, or add *Ketoconazole* powder to the mortar. Dissolve the *Cetylpyridinium Chloride* in *Purified Water*, and dilute quantitatively, and stepwise if necessary, with *Purified Water* to obtain 10 mL of a solution containing 10 mg of *Cetylpyridinium Chloride*. Transfer this solution, in divided portions, to the mortar containing the powder, and mix to form a smooth paste. Place 20 mL of *Purified Water* in a beaker. Using moderate heat, stir to form a vortex, and slowly sprinkle the *Xanthan Gum* into the vortex to obtain a uniform dispersion. Add the dispersion to the wetted powder paste, and mix until smooth. Add a sufficient quantity of the *Suspension Structured Vehicle* or *Sugar-Free Suspension Structured Vehicle* to bring to final volume. Mix well.

**ASSAY**

• **Procedure**

**Mobile phase:** Acetonitrile and 0.01 M tetrabutylammonium hydrogen sulfate (25:75). Pass through a filter of 5-µm or finer pore size, and degas.

**Diluent:** Methanol and water (50:50)

**System suitability solution:** Dissolve 4 mg of USP Ketoconazole RS in 1.0 mL of a solution of potassium sorbate in water (1 in 5000). Dilute with *Diluent* to 10.0 mL.

**Standard solution:** 0.4 mg/mL of USP Ketoconazole RS in *Diluent*

**Sample solution:** [Note—If the Oral Suspension has settled, invert the container 10–15 times, and sonicate for 5 min, or stir on a magnetic stirrer until the Oral Suspension appears homogeneous. Examine the mixture for the presence of bubbles and unsuspended solids before sampling.] Transfer 5.0 mL of homogeneous Oral Suspension to a 250-mL volumetric flask, add 100 mL of water, and stir for 15 min to dissolve the xanthan gum. Add 135 mL of methanol, and stir for an additional 15 min. Cool, and dilute with methanol to volume.

**Chromatographic system**

(See *Chromatography ⟨621⟩, System Suitability*.)

**Mode:** LC

**Detector:** UV 223 nm

**Columns**

**Guard:** 5-µm packing L1

**Analytical:** 4.6-mm × 25-cm; 5-µm packing L1

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection volume:** 5 µL

**System suitability**

**Samples:** *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for ketoconazole and sorbate are 1.0 and 1.7, respectively.]

**Suitability requirements**

**Resolution:** NLT 2.0 between sorbate and ketoconazole, *System suitability solution*

**Relative standard deviation:** NMT 2.0% for replicate injections, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ketoconazole ($C_{26}H_{28}Cl_2N_4O_4$) in the portion of Oral Suspension 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)

$C_U$ = nominal concentration of ketoconazole in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

## ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Package in tight, light-resistant containers. Store at controlled room temperature.
- **BEYOND-USE DATE:** NMT 14 days after the date on which it was compounded when stored at controlled room temperature
- **LABELING:** Label it to state that it is to be well shaken before use, and that it is to be protected from light. Label it to state the *Beyond-Use Date.*
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Ketoconazole RS

**Auxiliary Information** - Please check for your question in the FAQs before contacting USP.

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| KETOCONAZOLE COMPOUNDED ORAL SUSPENSION | Brian Serumaga<br>Science Program Manager | CMP2020 Compounding 2020 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | CMP2020 Compounding 2020 |

**Chromatographic Database Information:** Chromatographic Database

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