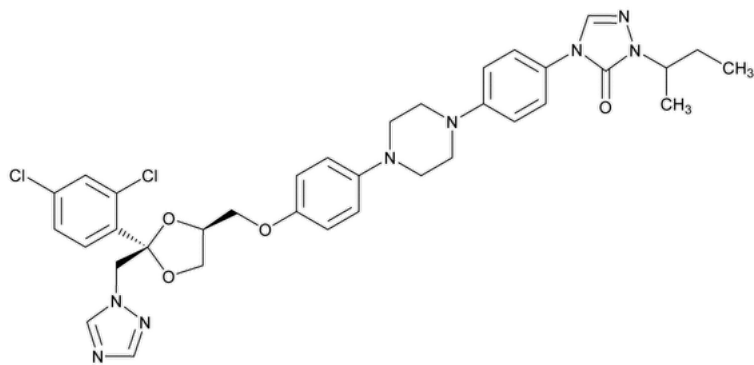


Status: Currently Official on 18-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-DEF4FB08-751A-4EB2-A94B-0FEE17605BA3_4_en-US
DOI: https://doi.org/10.31003/USPNF_M43724_04_01
DOI Ref: 5a0pe

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Itraconazole



$C_{35}H_{38}Cl_2N_8O_4$ 705.63
3*H*-1,2,4-Triazol-3-one, 4-[4-[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]phenyl]-2,4-dihydro-2-(1-methylpropyl)-; (±)-1-sec-Butyl-4-[*p*-[4-[*p*-[[2-(2*R**,4*S**)-2-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]phenyl]-Δ²-1,2,4-triazolin-5-one CAS RN®: 84625-61-6; UNII: 304NUG5GF4.

DEFINITION
Itraconazole contains NLT 98.0% and NMT 102.0% of itraconazole ($C_{35}H_{38}Cl_2N_8O_4$), calculated on the dried basis.

IDENTIFICATION
Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy: 197K* ▲ (CN 1-MAY-2020)
- **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
• **PROCEDURE**

Prepare the solutions containing itraconazole immediately before use.

Solution A: 13.6 g/L of [tetrabutylammonium hydrogen sulfate](#) in [water](#)

Solution B: Acetonitrile

Diluent: Dilute 4.0 mL of [hydrochloric acid](#) with methanol to 1 L.

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
12	50	50
16	80	20
20	80	20

Standard solution: 0.3 mg/mL of [USP Itraconazole RS](#) in *Diluent*

Sample solution: 0.3 mg/mL of Itraconazole 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](#)

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of itraconazole ($C_{35}H_{38}Cl_2N_8O_4$) in the portion of Itraconazole taken:

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

r_U = peak response of itraconazole from the *Sample solution*

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

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

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

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

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#)

Sample: 1.0 g

Acceptance criteria: NMT 0.1%

• ORGANIC IMPURITIES

Solution B, Diluent, and Chromatographic system: Proceed as directed in the Assay.

Solution A: 27.2 g/L of [tetrabutylammonium hydrogen sulfate](#) in [water](#)

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	80	20
2	80	20
22	50	50
27	50	50

System suitability solution: 10 mg/mL of [USP Itraconazole System Suitability Mixture RS](#) in *Diluent*

Standard solution: 10.0 μg/mL of [USP Itraconazole RS](#) in *Diluent*

Sample solution: 10 mg/mL of Itraconazole in *Diluent*

System suitability

Sample: *System suitability solution*

Suitability requirements

Peak-to-valley ratio: NLT 1.5

Calculate the peak-to-valley ratio (p/v), using the following:

$$p/v = H_p/H_v$$

H_p = height above the baseline of the peak due to the *n*-butyl isomer impurity

H_v = height above the baseline of the lowest point of the curve separating this peak from the itraconazole peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Itraconazole taken: