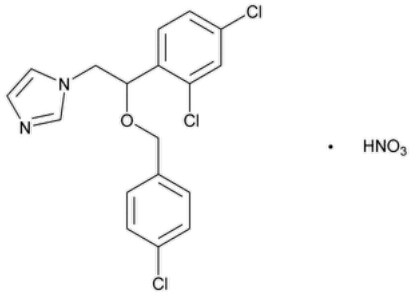
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Sep-2022
Document Type: USP Monographs
DocId: GUID-59F73D1C-AFA4-445B-A8BD-F21F645015B9_4_en-US
DOI: https://doi.org/10.31003/USPNF_M28900_04_01
DOI Ref: zh0zd

Econazole Nitrate



$C_{18}H_{15}Cl_3N_2O \cdot HNO_3$ 444.70

1*H*-Imidazole, 1-[2-[(4-chlorophenyl)methoxy]-2-(2,4-dichlorophenyl)ethyl]-, mononitrate, (±)-;

(±)-1-[2,4-Dichloro-β-[(*p*-chlorobenzyl)oxy]phenethyl]-imidazole mononitrate CAS RN®: 24169-02-6; UNII: H438WYN10E.

DEFINITION

Econazole Nitrate contains NLT 98.0% and NMT 102.0% of econazole nitrate ($C_{18}H_{15}Cl_3N_2O \cdot HNO_3$), 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*.
- **C.**

Sample solution: 10 mg with 5 mL of water

Analysis: Shake the *Sample solution*, and cool the resulting suspension in ice. Keeping the suspension cool, add 0.4 mL of potassium chloride solution (1 in 10), 0.1 mL of diphenylamine TS, and, dropwise with shaking, 5 mL of sulfuric acid.

Acceptance criteria: An intense blue color develops.

ASSAY

- **Procedure**

Solution A: 0.77 g/L of ammonium acetate in water

Solution B: Methanol and *Solution A* (20:80)

Solution C: Acetonitrile and methanol (60:40)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	60	40
25	10	90
27	10	90
27.1	60	40
30	60	40

Diluent: Methanol and water (40:60)

Standard solution: 0.4 mg/mL of USP Econazole Nitrate RS in *Diluent*. [Note—Sonication may be needed to dissolve the Standard.]

Sample solution: 0.4 mg/mL of Econazole Nitrate in *Diluent*. [Note—Sonication may be needed to dissolve the sample.]

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: 35°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of econazole nitrate ($C_{18}H_{15}Cl_3N_2O \cdot HNO_3$) in the portion of Econazole Nitrate taken:

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

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

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

C_S = concentration of USP Econazole Nitrate RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.02 mg/mL each of USP Econazole Related Compound A RS, USP Econazole Related Compound B RS, and USP Econazole Related Compound C RS, and 0.01 mg/mL of USP Econazole Nitrate RS in methanol

Sample solution: 10 mg/mL of Econazole Nitrate in methanol

System suitability

Sample: *Standard solution*

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between econazole related compound C and econazole

Relative standard deviation: NMT 3% for econazole related compound A, econazole related compound B, econazole related compound C, and econazole

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of econazole related compound A, econazole related compound B, or econazole related compound C in the portion of Econazole Nitrate taken:

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

r_U = peak response of econazole related compound A, econazole related compound B, or econazole related compound C from the *Sample solution*

r_S = peak response of econazole related compound A, econazole related compound B, or econazole related compound C from the *Standard solution*

C_S = concentration of USP Econazole Related Compound A RS, USP Econazole Related Compound B RS, or USP Econazole Related Compound C RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other unspecified impurities in the portion of Econazole Nitrate taken:

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

r_U = peak response of each impurity from the *Sample solution*

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

C_S = concentration of USP Econazole Nitrate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Econazole related compound A	0.2	0.375
Econazole related compound B	0.6	0.375
Econazole related compound C	0.8	0.375
Econazole	1.0	—
Any individual unspecified impurity	—	0.10
Total impurities	—	2.0

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from light.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Econazole Nitrate RS

USP Econazole Related Compound A RS

Deschlorobenzyl econazole;
1-(2,4-Dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanol.
$C_{11}H_{10}Cl_2N_2O$ 257.12

USP Econazole Related Compound B RS

Econazole amine;
2-[(4-Chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine nitrate.
$C_{15}H_{14}Cl_3NO \cdot HNO_3$ 393.65

USP Econazole Related Compound C RS

Econazole quarternary salt;
1-(4-Chlorobenzyl)-3-{2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl}-1*H*-imidazol-3-ium ▲chloride.
$C_{25}H_{21}Cl_5N_2O$ 542.71▲ (ERR 1-Sep-2022)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(2)

Current DocID: GUID-59F73D1C-AFA4-445B-A8BD-F21F645015B9_4_en-US

DOI: https://doi.org/10.31003/USPNF_M28900_04_01

DOI ref: zh0zd