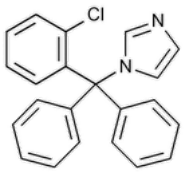
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-C04D415F-9F7B-4CB9-8044-1114A71710BE_4_en-US
DOI: https://doi.org/10.31003/USPNF_M18880_04_01
DOI Ref: 10c5f

Clotrimazole



$C_{22}H_{17}ClN_2$ 344.84

1*H*-Imidazole, 1-[(2-chlorophenyl)diphenylmethyl]-;

1-(*o*-Chloro-α,α-diphenylbenzyl)imidazole CAS RN®: 23593-75-1; UNII: G07GZ97H65.

DEFINITION

Clotrimazole contains NLT 98.0% and NMT 102.0% of $C_{22}H_{17}ClN_2$, calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (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**

Buffer: 4.35 mg/mL of dibasic potassium phosphate

Mobile phase: Acetonitrile and *Buffer* (3:1). Pass through a membrane filter having a 0.2-µm or finer pore size. The ratio of volumes may be changed to obtain the required resolution.

Standard solution: 0.5 mg/mL of USP Clotrimazole RS in methanol

System suitability solution: 0.1 mg/mL each of USP Clotrimazole RS and USP Clotrimazole Related Compound A RS in methanol

Sample solution: 0.5 mg/mL of Clotrimazole in methanol

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1.5 mL/min

Injection size: 25 µL

System suitability

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

[Note—The relative retention times for clotrimazole and clotrimazole related compound A are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2.0 between clotrimazole and clotrimazole related compound A, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{22}H_{17}ClN_2$ in the portion of Clotrimazole taken:

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

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

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

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

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

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

IMPURITIES

Inorganic Impurities

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

Organic Impurities

- **Procedure 1: Limit of Imidazole**

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Standard solution: 500 µg/mL of USP Imidazole RS in chloroform

Sample solution: 100 mg/mL of Clotrimazole in chloroform

Application volume: 5 µL

Developing solvent system: Methanol and chloroform (3:2)

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed for *Chromatography ⟨621⟩, Thin-Layer Chromatography*. After air-drying the plate for 5 min, place it in a closed container with a dish containing 100 g of iodine in a shallow layer, and allow to remain for 60 min. Remove the plate from the container, and observe the chromatogram.

Acceptance criteria: Any brown spot from the *Sample solution* at an R_F value corresponding to the principal spot from the *Standard solution* is not greater in size or intensity than the principal spot from the *Standard solution:* NMT 0.5% of imidazole.

- **Procedure 2: Limit of Clotrimazole Related Compound A**

Buffer, Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 50 µg/mL of USP Clotrimazole Related Compound A RS prepared by dissolving in methanol using about 75% of the final flask volume. Dilute with *Buffer* to volume.

Sample solution: Transfer 100 mg of Clotrimazole to a 10-mL volumetric flask, add 5 mL of methanol to dissolve, add 2.5 mL of *Buffer*, dilute with methanol to volume, and mix.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clotrimazole related compound A in the portion of Clotrimazole taken:

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

r_U = peak response of clotrimazole related compound A from the *Sample solution*

r_S = peak response of clotrimazole related compound A from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 2 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards ⟨11⟩**

USP Clotrimazole RS

USP Clotrimazole Related Compound A RS

(o-Chlorophenyl)diphenylmethanol.

$C_{19}H_{15}ClO$ 294.78

USP Imidazole RS

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(3)

Current DocID: GUID-C04D415F-9F7B-4CB9-8044-1114A71710BE_4_en-US
DOI: https://doi.org/10.31003/USPNF_M18880_04_01
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